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	INSTRUMENTATION
	OXYGENATORS
	EMERGENCY SYSTEM
	TEMPORARY SYSTEM
	PERMANENT SYSTEM
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	PHYSIOLOGY
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	CHEMISTRY
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	TEST AND EVALUATION
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	RESPIRATORY DEVICES

PREPARED FOR - THE BIOMATERIALS PROGRAM

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16. Abstracts

The primary goal of this program has been to characterize the engineering and biological properties of carbon-surfaced polymeric, metallic, and ceramic composites. A variety of engineering studies were carried out which established the adhesion, strain-to-failure, wear, fatigue, and fluid friction erosion characteristics of test specimens coated with a thin layer of isotropic (LTI-like) carbon. These studies, while not complete, have demonstrated that carbon-coated composites possess the necessary engineering properties for use in prosthetic devices. Coated test specimens were supplied for biological testing by collaborating contractors and others. The biological test results to date, taken as a whole, indicate that composites surfaced with thin isotropic carbon films exhibit biochemical properties similar to those of LTI carbon. As a service to other contractors, about 950 implant rings were processed. The injection mold was completed. Implant rings were molded from five different polymers.

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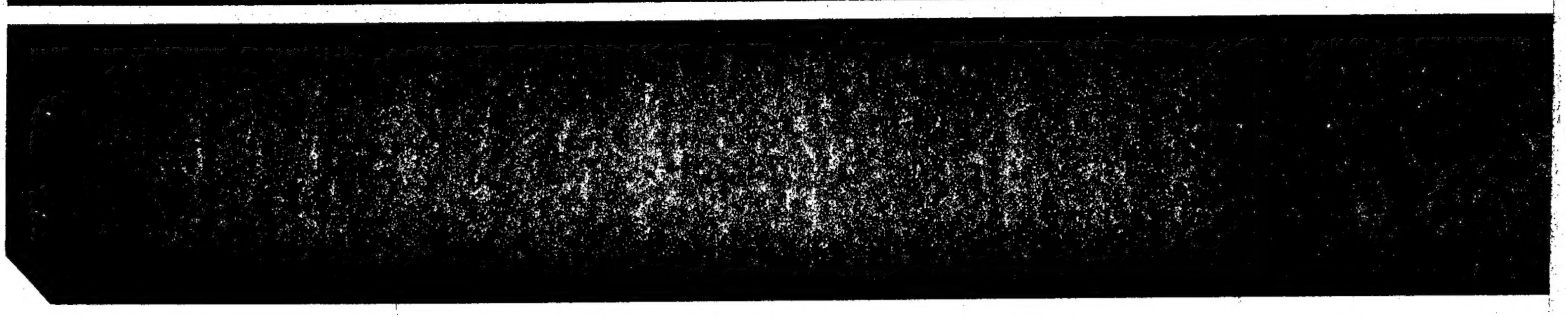

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SUMMARY

The overall goal of this project is the characterization and evaluation of carbon-surfaced polymeric, metallic, and ceramic composites for use in prosthetic devices with particular emphasis on determining the engineering and biological properties of materials surfaced with thin carbon films.

A particular form of carbon, namely, low-temperature isotropic pyrolytic carbons (LTI carbons), has found wide applications in prosthetic devices not only because LTI carbons are inherently thromboresistant and biologically inert but also because their physical and mechanical properties are tailorable to fit the applications. The primary goals of the current research have been to determine whether thin carbon films that have physical and chemical properties similar to those of LTI carbons also confer the biochemical properties of LTI carbons to the coated composites and to determine the engineering properties of these carbon-surfaced composites. Other, equally important goals are to further biomaterials research and information exchange by collaborating with other contractors and to supply well-characterized accepted materials for basic scientific studies. As a separate part of this contract, standard well-characterized molded implant rings were supplied as a service to other NHLBI contractors.

The precise mechanisms responsible for the biological acceptability demonstrated by LTI carbons are not well understood, but the physical and chemical properties of these materials are well known. As a starting point in the investigation of carbon-surfaced composites, we have shown that the physical and chemical properties of thin vapor-deposited carbon films can be tailored to resemble the measured properties of LTI carbons. Furthermore, we have quantified some of the engineering properties necessary to allow inclusion of carbon-surfaced composites in prosthetic devices. We have shown, for example, that thin carbon films are immune to dynamic fatigue.

Carbon-surfaced composites are not susceptible to fluid friction erosion in laminar flow or turbulent flow. The films bond well to a variety of materials. We have begun to study the wear behavior of these composites and to determine the strain-to-failure of carbon-surfaced polymeric composites. Knowledge of these properties is necessary for the design and fabrication of devices. Without the necessary mechanical properties, even the most biocompatible material would be of little value in prosthetics.

A variety of tests have been and are being performed to determine the biological properties of materials surfaced with thin carbon films. Most of these tests are being performed by collaborating NHLBI contractors according to their respective protocols. Carbon-surfaced implant rings perform well in the inferior vena cava and when tested according to the renal embolus protocol. They do not violently attract cellular elements from blood. Other experiments indicate that thin carbon films indeed confer the biochemical properties of carbon to the substrate. Clot formation and clot composition on carbon-surfaced shafts are considerably smaller than that on uncoated shafts, according to the University of Michigan. In earlier studies at the University of Michigan, it was found that carbon-coated nylon microfiber scaffolds were excellent substrates for cellular growth leading to the formation of pseudointimas. Cells would not grow on the uncoated substrate. The deposition of cellular blood elements in nickel microchannels was found to be significantly greater than that on microchannels coated with a thin, isotropic carbon film. The deposition of platelets was found to be smaller by a factor of 2 on coated glass cover slips than that on the reference polyether urethane (PEU) used at Columbia University in these experiments. Additional testing is in progress, since no single biological test determines the acceptability of a material and since materials used to advantage in a specific application may be unsuitable in others. Tests of carbon-surfaced composites in specific applications are also under way. The test data available to date, taken as a whole, show that carbon-surfaced composites do have the potential of complementing LTI carbons as bioimplant materials and have the necessary physical properties to be useful in prosthetic devices.

As a service to other NHLBI contractors, we have supplied approximately 950 implant rings during the present reporting period. The injection mold was completed. Rings were molded from Pellethane-D, polypropylene, polycarbonate, ethylene/vinyl acetate, and polysulfone.

TASK I. INVESTIGATION OF VACUUM-DEPOSITED CARBON COATINGS

1.1. Summary of Activities

We have placed major emphasis on characterizing test specimens and on compiling the engineering properties necessary for the use of carbon-coated composites in prosthetic devices. Determination of the fatigue behavior of carbon-coated metal composites has been completed, and a paper has been submitted to the Journal of Bioengineering for publication.* Carbon-coated metal composites do not fail in fatigue provided that the elastic strain limit of the metal is not exceeded. Determination of the fatigue behavior of carbon-coated polymeric composites is under way. A brief communication on the wear behavior of vacuum-vapor-deposited carbon has also been submitted to the Journal of Bioengineering. The adhesion of carbon films to carbide-forming metals is on the order of 5000 psi and is lower in the case of noncarbide formers. A paper on the resistance of carbon-coated composites to fluid friction erosion is being prepared for publication. An apparatus to study the strain-to-failure of polymeric composites has been completed. This apparatus will also be used to study the mechanical behavior of carbon-coated prosthetic fabrics. Initial results from galvanic corrosion experiments indicate that carbon/stainless steel composites should not be used in vivo. Carbon/titanium (or titanium alloy) composites, however, are not susceptible to galvanic corrosion in simulated body fluids.

1.2. Characterization

During the present reporting period, carbon-coated metallic and polymeric composites were characterized for use and study at General Atomic (GA) and by collaborating NHLBI contractors. The specimens used at GA were primarily of the type and configuration required by specific tests to determine the engineering properties of the composites. The specimens

*A list of publications during the present reporting period based in part on work supported by this contract can be found in Appendix A.

sent to collaborating contractors were primarily intended for biological testing. These specimens are described in subsequent sections of this annual report. The characterization techniques used included optical and scanning electron microscopy, electron microprobe spectroscopy, and Auger electron spectroscopy. Recently, through collaborative efforts with the University of Utah and the University of Pittsburgh, coated composites have been analyzed using ESCA, SIMS, ISS, and FITR before and after exposure to blood. A paper on the initial results from these studies was presented at the Scanning Electron Microscopy Symposium in Los Angeles (April 1978) and will be published in the symposium proceedings.

1.3. Adhesion

The bond strength of thin carbon films on a variety of materials was previously studied and reported (Ref. 1). Bond strengths greater than 5100 psi were achieved for both the carbon/stainless steel and the carbon/titanium systems. These high bond strengths were thought to be a result of the formation of a reactive interface between the carbon film and the metals; i.e., it was found that the carbon spectrum in Auger composition depth profile changed its shape from one characteristic of pure carbon at the surface to one indicative of carbide at the carbon/metal interface. The carbon films on Vespel (SP-1), a polyimide material, debonded, with the strength ranging from about 2860 psi to about 3700 psi. The debonding mode in the carbon/Vespel specimens was mixed. In some specimens, failure occurred not only at the carbon film/Vespel interface but also in the bulk of the Vespel. In other specimens, failure occurred entirely in the bulk of the Vespel, indicating that bond strengths which exceed the bulk strength of the Vespel itself can be achieved. Some of these results were presented at the 13th Biennial Conference on Carbon in Irvine, California (July 1977), and a paper on the most recent results was presented at the 4th Annual International Biomaterials Symposium in San Antonio, Texas (April 1978).

Since the excellent bond strength of carbon films on stainless steel was thought to be a result of the formation of a carbide-like reactive interface, it was decided to test the bond strength of carbon films on a noncarbide-forming metal such as platinum. In the previous annual report

(Ref. 1), results from two sets of carbon/platinum specimens were described. Except for one specimen which debonded cleanly at the carbon/platinum interface, all specimens failed at the epoxy joint, with the strength ranging from about 3086 psi to about 3762 psi. The bond strength calculated from the cleanly debonded specimen was about 4421 psi. During the present reporting period, two more sets of carbon/platinum specimens (No. 516771 and 415771) were tested (see Table 1-1). In all specimens, the failure occurred at the epoxy joint, with an average strength of 2930 psi for one set and 4089 psi for the other set. At any rate, the bond strengths observed from the carbon/platinum systems are exceptionally high for a noncarbide-forming metal. An attempt to determine the adhesion mechanism, i.e., the chemical nature of the carbon/platinum interface, was made by using Auger electron spectroscopy. This experiment was not entirely successful because one of many peaks in the platinum Auger spectrum overlapped the characteristic carbon peak and made it difficult to extract the exact shape of the carbon spectrum at the interface.

Because of the difficulty encountered in Auger analysis for the platinum substrate, oxygen-free high-conductivity copper (99.999% pure), another noncarbide-forming metal, was chosen as an alternative substrate material. The coupons were made from highly polished sheet stock, coated with carbon films, and tested by using the method previously employed (Ref. 1). The results are summarized in Table 1-1. The specimens in the first two lots (No. 125772 and 1111774) either completely debonded at the epoxy joint or partially debonded at the intended interface, i.e., the carbon/copper interface. The average strength for these lots was about 1340 and 1721 psi, respectively. Almost all of the specimens in the remaining lots (No. 923771, 922772, 99771, and 826771) debonded cleanly at the carbon/copper interface. The average strength for these lots was calculated to be 1721, 1728, 1874, and 1562 psi, respectively. The bond strengths of the carbon/copper specimens, which range from 1340 to 1874 psi, are much lower than those of other carbon/metal systems and are attributable to the absence of a reactive interface between the carbon film and the copper. The composition depth profile made by Auger electron spectroscopy indicates that not only does the shape of the carbon spectrum remain unchanged but also the carbon

TABLE 1-1
BOND STRENGTH OF CARBON FILMS ON VARIOUS SUBSTRATES

Specimen Identification Number(a)	Substrate Material	Measured Load at Failure, lb(b)	Calculated Bond Strength, psi	Debonded at Interface of
516771-1	Platinum	175	3565	Substrate/specimen grip
-2	Platinum	156	3178	Substrate/specimen grip
-3	Platinum	188	3830	Substrate/specimen grip
-4	Platinum	210	4278	Substrate/specimen grip
-5	Platinum	265	5399	Substrate/specimen grip
-6	Platinum	210	4278	Substrate/specimen grip
415771-1	Platinum	130	2648	Substrate/specimen grip
-2	Platinum	144	2934	Substrate/specimen grip
-3	Platinum	122	2458	Substrate/specimen grip
-4	Platinum	123	2506	Substrate/specimen grip
-5	Platinum	191	3891	Substrate/specimen grip
-6	Platinum	100	3117	Substrate/specimen grip
125772-1	Copper	75 (90)	1698	Carbon film/substrate
-2	Copper	58 (99)	1194	Carbon film/substrate
-3	Copper	50 (95)	1072	Carbon film/substrate
-4	Copper	65 (95)	1394	Carbon film/substrate
-5	Copper	TNV(c)	TNV(c)	TNV(c)
-6	Copper	TNV(c)	TNV(c)	TNV(c)
1111774-1	Copper	87 (95)	1865	Carbon film/substrate
-2	Copper	84 (95)	1801	Carbon film/substrate
-3	Copper	95	1935	Substrate/specimen grip
-4	Copper	87	1772	Substrate/specimen grip
-5	Copper	70	1426	Substrate/specimen grip
-6	Copper	75	1528	Substrate/specimen grip
923771-1	Copper	84(d)	1711	Carbon film/substrate
-2	Copper	82(d)	1670	Carbon film/substrate
-3	Copper	67(d)	1365	Carbon film/substrate
-4	Copper	96(d)	1956	Carbon film/substrate
-5	Copper	90(d)	1833	Carbon film/substrate
-6	Copper	102(d)	2078	Carbon film/substrate
922772-1	Copper	81(d)	1650	Carbon film/substrate
-2	Copper	62(d)	1263	Carbon film/substrate
-3	Copper	59(d)	1202	Carbon film/substrate
-4	Copper	92(d)	1874	Carbon film/substrate
-5	Copper	109(d)	2220	Carbon film/substrate
-6	Copper	106(d)	2159	Carbon film/substrate

(a) Code denotes the deposition lot number and the specimen number.

(b) Numbers within parentheses indicate % area debonded.

(c) Test not valid

(d) Complete debonding at intended interface

TABLE 1-1 (continued)

Specimen Identification Number[a]	Substrate Material	Measured Load at Failure, lb[b]	Calculated Bond Strength, psi	Debonded at Interface of
99771-1	Copper	87[d]	1772	Carbon film/substrate
-2	Copper	96[d]	1956	Carbon film/substrate
-3	Copper	100[d]	2037	Carbon film/substrate
-4	Copper	76[d]	1548	Carbon film/substrate
-5	Copper	100[d]	2037	Carbon film/substrate
-6	Copper	93[d]	1895	Carbon film/substrate
826771-1	Copper	66[d]	1345	Carbon film/substrate
-2	Copper	90[d]	1833	Carbon film/substrate
-3	Copper	90[d]	1833	Carbon film/substrate
-4	Copper	74[d]	1508	Carbon film/substrate
-5	Copper	66	1345	Substrate/specimen grip
-6	Copper	74[d]	1058	Carbon film/substrate

[d]Complete debonding at intended interface

signal rapidly drops to zero at the interface without revealing any interdiffusion-type layer. The Auger spectra at the surface and at a point close to the interface are shown in Fig. 1-1. The low-energy (60-eV) and the 920-eV major peaks characteristic of copper Auger electrons and the 272-eV carbon peak are clearly visible in Fig. 1-1(b). Further depth profiling showed that the carbon signal rapidly disappeared. The estimated interfacial region was about 100 Å. The bond strength observed with the carbon/copper system is, therefore, most likely a result of mechanical interlocking between the carbon film and the copper, and since the copper coupons were highly polished, mechanical interlocking was probably minimized.

In summary, the carbon films on the carbide-forming metals such as stainless steel and titanium exhibited an excellent bond strength, equal to or greater than about 5000 psi. The carbon films on a copper substrate, a noncarbide-forming metal, resulted in a bond strength of only about 1700 psi. However, the bond strength of carbon films on platinum, another noncarbide-forming metal, was on the order of 3000 to 4000 psi (or possibly 4400 psi). Whether this adhesion is achieved via an unidentified reactive interface is yet to be determined. The adhesion of carbon films to Vespel was also interesting. The average calculated bond strength ranged from about 2860 psi to about 3700 psi, i.e., comparable to or greater than the strength

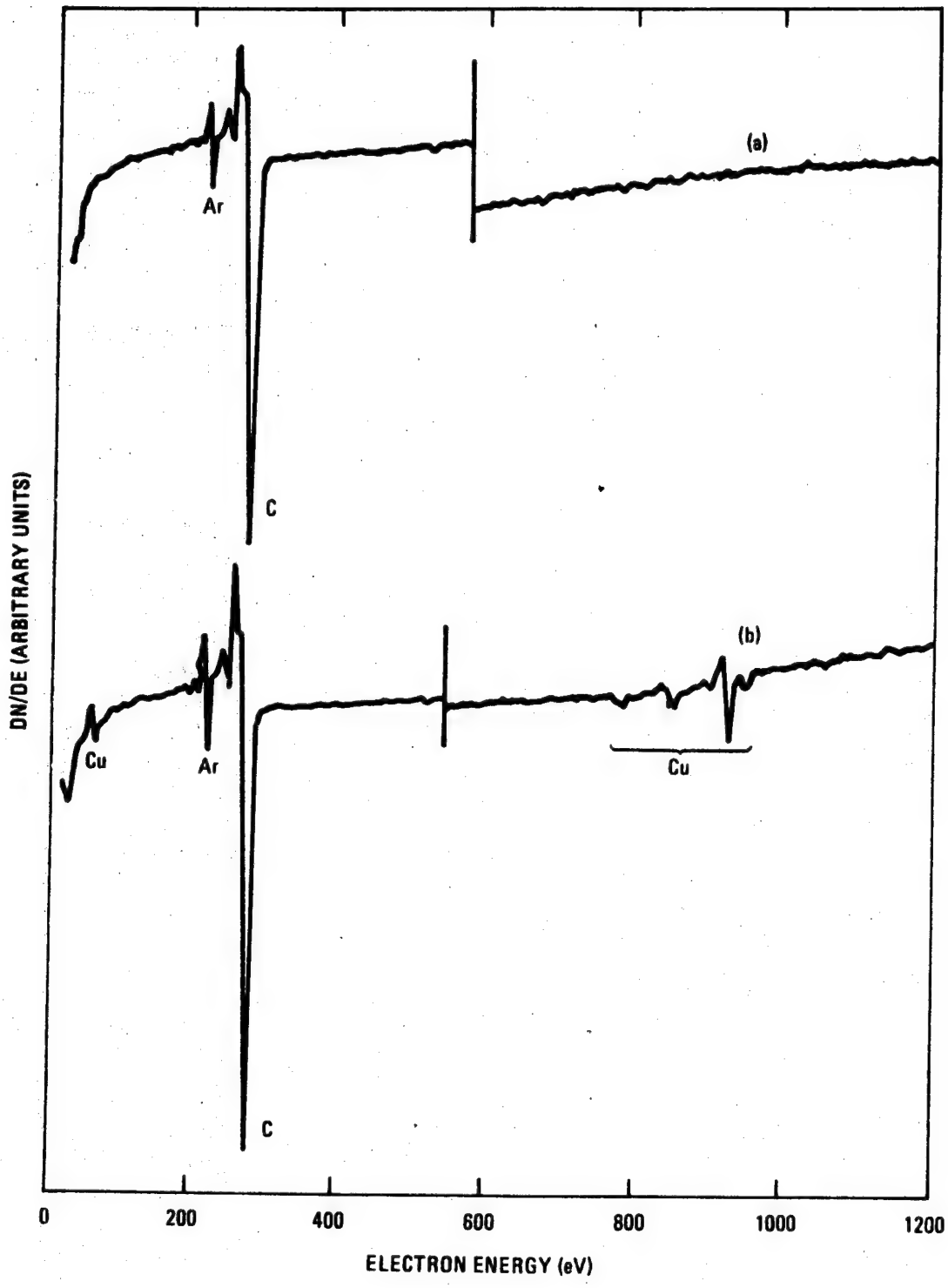

Fig. 1-1. Auger spectra from carbon-coated copper adhesion test specimen: (a) at the surface; (b) at a point close to the interface

of the bulk polymer itself. The adhesion mechanism responsible for this high bond strength is not understood at the present time but may be a result of covalent bonding between the carbon films and the polymer.

1.4. Fatigue

The fatigue characteristics of carbon films on stainless steel have been studied and reported previously (Ref. 1). The results indicated that the fractures in the carbon film always coincided with the onset of plastic deformation in the substrate. In other words, the carbon films fractured if and only if there had been severe deformation in the substrate, and no carbon film failed prior to substrate failure. The strain level in the specimen at which cracks started developing in the carbon film was very close to the elastic strain limit of the substrate. The failure in the carbon film would have occurred at a much higher strain if the substrate had a higher elastic strain limit. Some of the results of the carbon/metal composite fatigue study were also presented at the 13th Biennial Conference on Carbon. A paper on the fatigue behavior of vapor-deposited carbon films has been prepared (Ref. 2) and submitted to the Journal of Bioengineering for publication. A study of the fatigue behavior of carbon films on a polymeric substrate (e.g., Lexan, MR-9034, General Electric) was begun during the past reporting period. According to information provided by the manufacturer, the elastic strain limit of this material is about 2×10^{-2} (or 2%). Tensile coupons indentical in shape to the stainless steel coupons were cut from Lexan sheet (0.015 in. thick) and inspected under a polariscope and a microscope for gross defects. To understand the fatigue behavior of the substrate itself, defect-free substrates were tested at an initial strain level of 6.25×10^{-3}, using the same method employed with the carbon/stainless steel composites. Before and during the test, the alignment of the substrate with the tensile axis was checked by observing the stress patterns (or fringes) with polarized light. The test results were, however, not straightforward; i.e., the majority of specimens survived to 10^6 cycles, although minute edge cracks developed along the gage section of several specimens. Some specimens failed prematurely, which might have been a result of defects that passed unnoticed in both the polarized light and the microscopic examination.

During the present reporting period, several carbon-coated polycarbonate specimens have been tested in fatigue, again using 6.25×10^{-3} as the initial strain level in the specimen (see Table 1-2). At this approximate strain level, the carbon-coated stainless steel composites failed as early as 13,500 cycles. The data in Table 1-2 reveal that all carbon-coated specimens failed at low cycles ranging from about 50,000 cycles to about 82,000 cycles. These results are in contrast to those of the uncoated specimens, the majority of which survived to 10^6 cycles. The most plausible explanation is misalignment of the specimens under loading. The stress patterns (or fringes) in uncoated specimens, which are optically translucent, were easily observed with a polariscope so that the alignment could also be achieved easily. The carbon-coated specimens, however, are opaque, and consequently it was very difficult to align the specimens. For this reason, an extensive modification was made to the load train components so that, without relying upon observation of the stress patterns, the specimen could be aligned precisely. This modification has been completed, and testing has been resumed. It should be pointed out that the failures in the carbon-coated polycarbonate specimens, like those in the carbon-coated stainless steel composite specimens, occurred as a result of fatigue failure in the substrate.

As described above, Lexan seems to be very sensitive to misalignment and therefore may not be a proper substrate material for this study. For this reason, a stronger polymer (e.g., 6/6 nylon) has been obtained, and tensile coupons are being fabricated.

1.5. Fluid Friction Erosion

Carbon films on metallic and polymeric substrates are not susceptible to fluid friction erosion in either laminar flow or turbulent flow. Similar results were obtained by the Jet Propulsion Laboratory (JPL) in an independent study with a different erosion test apparatus (e.g., rectangular channel at GA and rotating disk at JPL). A manuscript that summarizes these results is being prepared for publication.

TABLE 1-2
FATIGUE EXPERIMENTS WITH CARBON-COATED POLYCARBONATE COMPOSITES

Specimen Identification Number	First Indication of Fatigue	Remarks
112771-1	Large edge crack at gage, 5.04×10^4 cycles	Failed at 5.04×10^4 cycles
112771-2	Large edge crack at gage, 7.56×10^4 cycles	Failed at 7.56×10^4 cycles
112771-3	Large edge crack at gage, 7.45×10^4 cycles	Failed at 7.45×10^4 cycles
516772-1	None	Failed at 6×10^4 cycles
516772-2	Large crack at round edge, 3×10^4 cycles	Failed at 6×10^4 cycles
516772-3	None	Failed at 4.9×10^5 cycles
516772-4	None	Failed at 7.67×10^4 cycles
516772-5	None	Failed at 8.24×10^4 cycles

1.6. Wear Behavior

A brief communication on the wear behavior of vacuum-vapor-deposited carbon films has been prepared (Ref. 3) and submitted to the Journal of Bioengineering for publication. This study has demonstrated that, when the properties of vacuum-vapor-deposited carbon are made similar to those of LTI carbon, the wear resistance of the two also becomes similar.

1.7. Strain-to-Failure

In earlier studies (Ref. 4), carbon films deposited on a polymeric substrate exhibited a much higher fracture strain (5% or greater) than did carbon films deposited on a rigid metallic substrate (2.4%). This high fracture strain has a significant implication because carbon films may be used as a coating on medical devices, many of which are made of polymeric materials and may be subject to some degree of strain during their use. During the present reporting period, experiments were undertaken to study systematically the fracture strain of thin carbon films on a variety of

polymeric substrates and to determine whether the tensile properties of these polymers are modified as a result of coating. An apparatus has been constucted and calibrated, and preliminary testing has been conducted.

A multipurpose, minitensile test apparatus being used in this study is shown in Fig. 1-2. The test system has three major components: load train, X-Y chart recorder, and macrophoto camera. The load train consists of specimen grips, a precision load cell, and a displacement transducer (see Fig. 1-3). One of the specimen grips is attached to a frictionless plane-type crossed-roller-bearing slide assembly, which is driven by a high-torque motor. Also connected to this slide assembly is a displacement transducer so that the amount of displacement in the specimen can be monitored. The other specimen grip is attached to the load cell so that, like the displacement, the load imposed on the specimen during extension can be monitored. The outputs from the load cell and the displacement transducer (i.e., load vs displacement curve) are recorded on the X-Y chart recorder. The macrophoto camera is used to record the displacement of the specimen at various stages of extension. The maximum load cell capacity and the crosshead speed are 50 lb and 0.080 in./min, respectively.

Tensile coupons were prepared from polycarbonate sheet stock (Lexan, MR-9034, General Electric, 0.020 in. thick), inspected for gross defects under a polarized light, coated with carbon film (about 5000 Å thick), and marked with fiducial points. The geometrical configuration of a typical specimen including fiducial points is schematically shown in Fig. 1-4. In the earlier studies (Ref. 4), the specimens were prepared by depositing carbon films onto polyimide-coated stainless steel coupons; i.e., polyimide/stainless steel composites were the substrate.

When a specimen such as that depicted in Fig. 1-4 is being strained, the majority of the specimen deformation occurs in the gage section, i.e., the distance between A and A in Fig. 1-4. Consequently, failure in the carbon film should appear somewhere on the gage section. In order to estimate better the amount of strain in the precise portion of carbon film/polymer composite where failure occurred, the changes in the distance between the fiducial marks (e.g., A'-A', B'-B', and C'-C') were measured

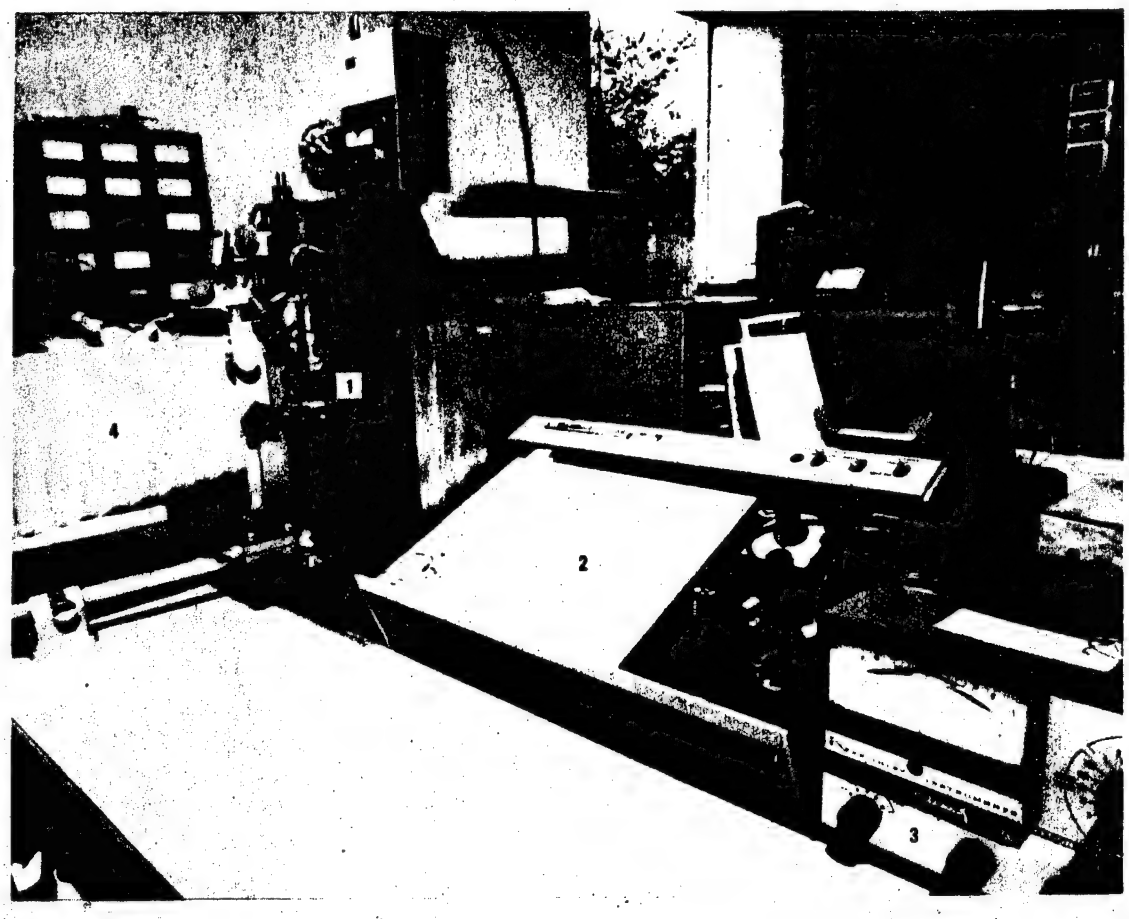

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Fig. 1-2. Overall view of strain-to-failure apparatus:

1 = load train
2 = X-Y chart recorder
3 = preamplifier for recorder
4 = macrophoto camera

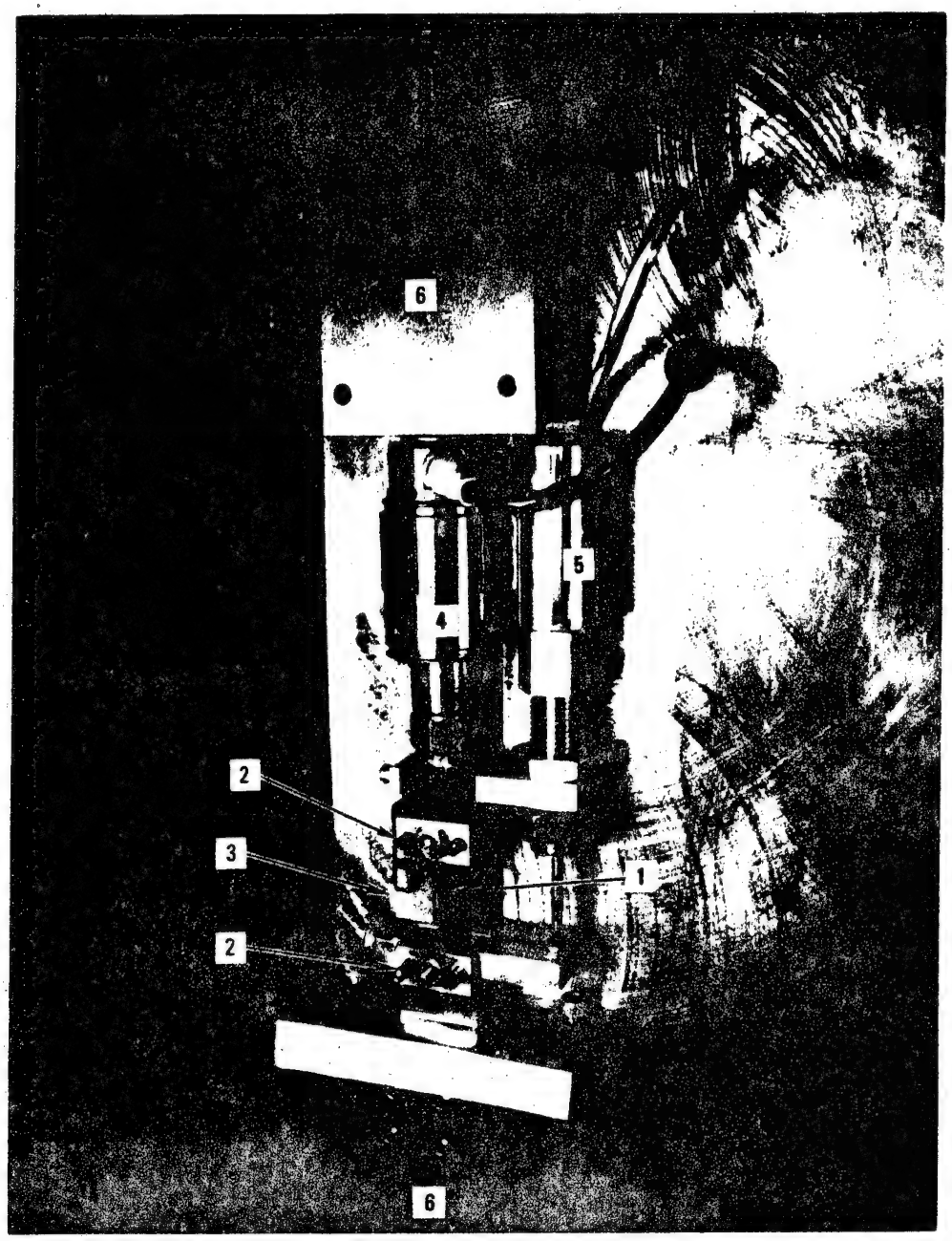

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Fig. 1-3. Closeup view of load train:

1 = specimen
2 = specimen grips
3 = precision reticle
4 = load cell
5 = displacement transducer
6 = plane-type crossed-roller bearings

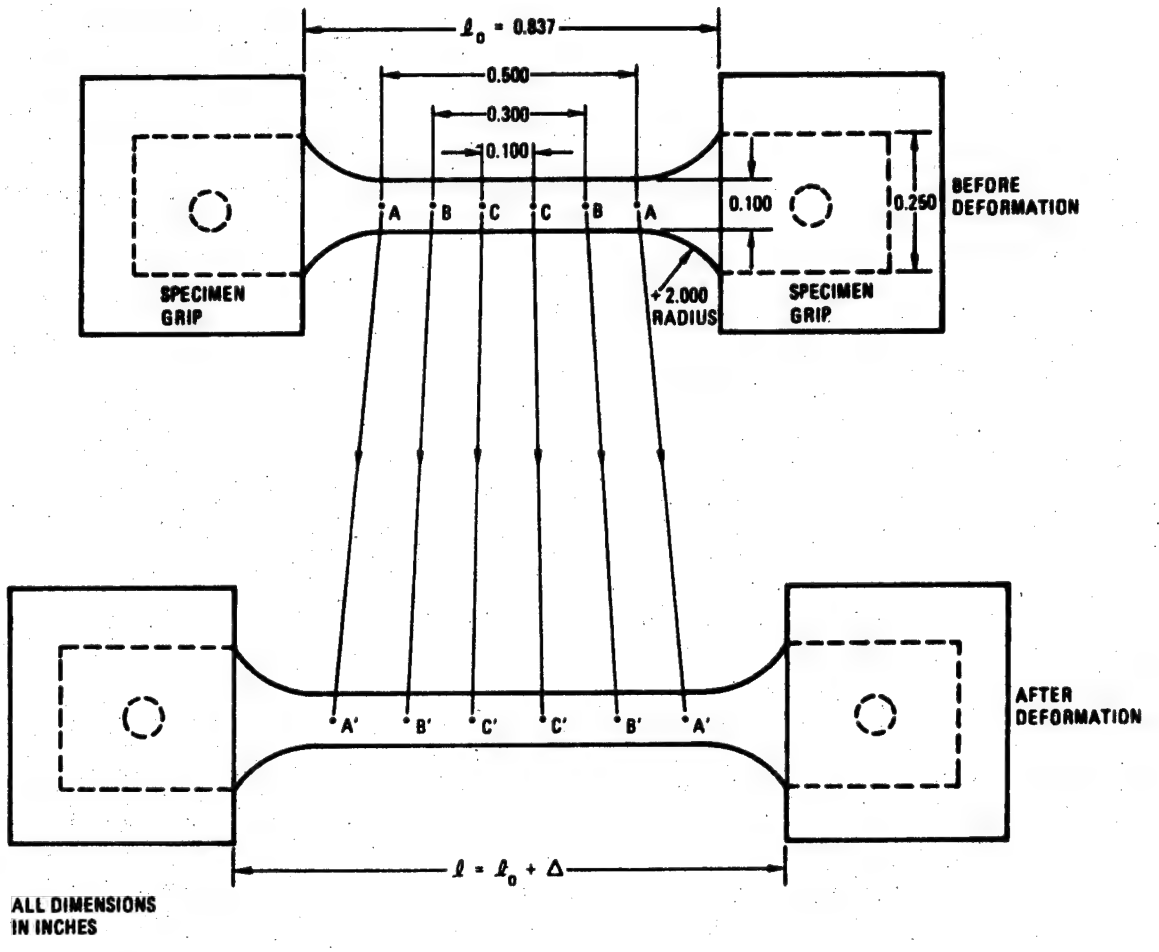

Fig. 1-4. Schematic diagram illustrating the geometrical configuration of a specimen in tensile grips: ℓ_o = original distance between the two grips (0.837 in.); A-A = original gage length

as a function of Δ, the displacement between the two tensile grips. Measurements were made in the following way. First, at each Δ increment of 0.010 in., the apparatus was completely stopped and the changes were measured using a Gaertner cathetometer. This method, however, had a severe drawback. During such measurements, the specimen creeps, which may or may not have an effect on reading the fiducial marks. Consequently, a second method was developed in which a series of photographs was taken while the specimen was continuously strained at a crosshead speed of 0.020 in./min. Also included in the photographs was a precision reticle (0.010 in./division) solidly fixed next to the specimen. By using the reticle as reference and with the aid of a toolmaker's microscope, the amount of strain in the specimen was accurately determined.

Plotted in Fig. 1-5 are the preliminary data showing the relationship between the amount of strain between the fiducial points and the crosshead displacement (Δ). The data indicate that the highest strain does occur at the middle section of the specimen (e.g., C'-C') and is about 20% higher than that at the gage length (e.g., A'-A'). A relationship of the sort described in Fig. 1-5 is useful because the amount of strain distributed in the gage section of the specimen is readily obtainable from the crosshead displacement without the use of cumbersome strain gages. An example is given in Table 1-3. By carefully examining the amount of strain in the various sections, it can readily be seen that permanent plastic deformation in the substrate occurs at about Δ = 0.040 in. For instance, up to Δ = 0.030 in., the strain in section C'-C' is the highest, in section B'-B' the second highest, and in section A'-A' the lowest, as would be expected from an elastically deformed tensile specimen. At Δ = 0.040 in., however, the highest strain is found in section B'-B', indicating that plastic deformation occurred in that section. By further comparing the amount of strain in section B'-B' with that in section C'-C', it can conclusively be inferred that plastic deformation occurred in sections B'-C' and C'-B' (see Fig. 1-4). Conventionally speaking, carbon film failure was accompanied by the plastic deformation in the substrate which occurred at a strain of about 5.7% (based on the conventional gage length), but, in reality, the fracture strain of the carbon film is more likely to be close to or greater than 6.4%.

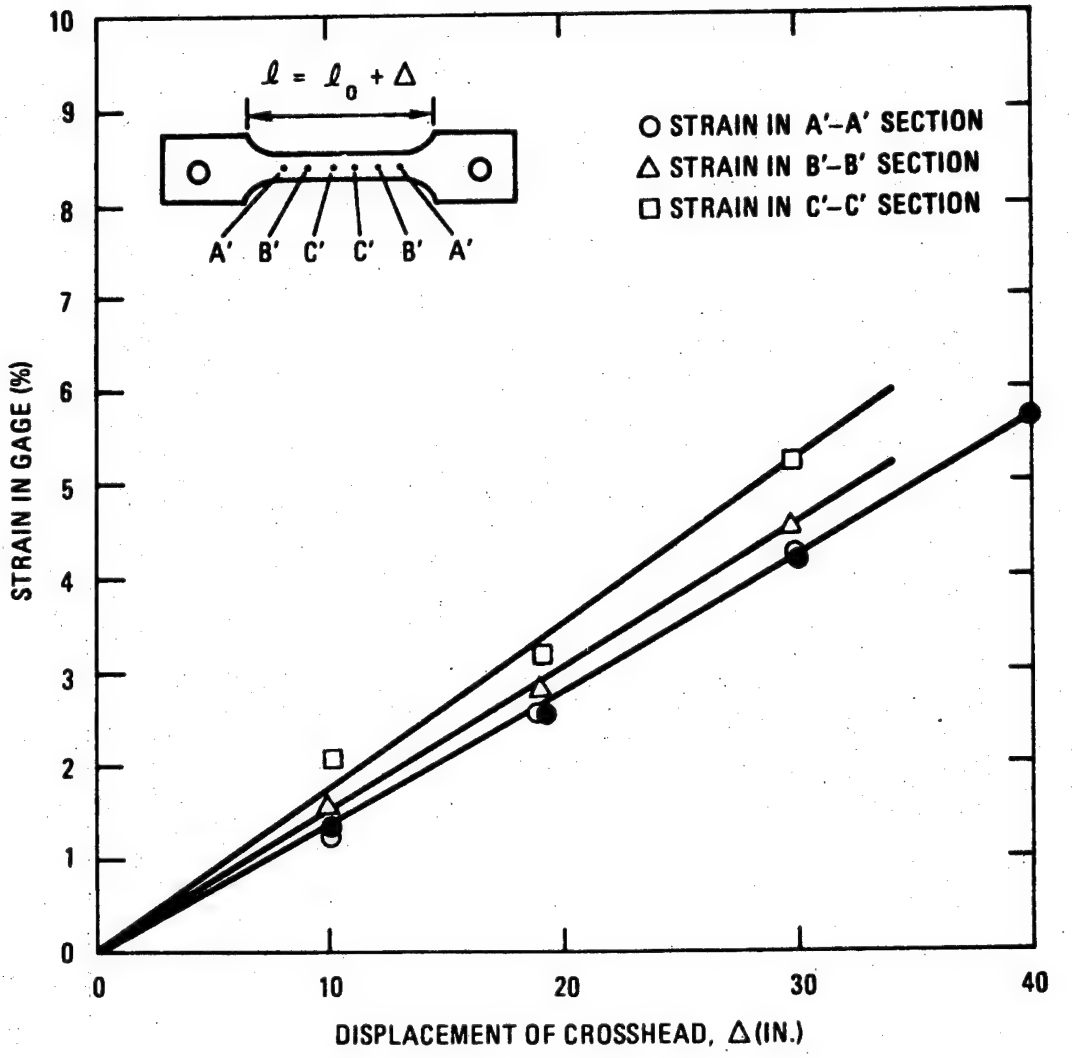

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Fig. 1-5. Percentage of strain in a specimen between pairs of fiducial points as a function of crosshead displacement. ℓ_0 = 0.837 in. Open points and closed points were obtained by cathetometer and photographic methods, respectively.

TABLE 1-3
CHANGES IN DISTANCE BETWEEN FIDUCIAL POINTS AS A FUNCTION OF CROSSHEAD DISPLACEMENT
(SPECIMEN NO. 6851-41)

Crosshead Displacement, Δ (in.)	Distance between Fiducial Points (in.)[a]		
	A'-A'[b]	B'-B'[b]	C'-C'[b]
0	0.5006	0.2966	0.1013
10	0.5069 (1.258)	0.3013 (1.585)	0.1033 (1.974)
20	0.5137 (2.609)	0.3055 (2.987)	0.1042 (2.863)
30	0.5217 (4.215)	0.3102 (4.585)	0.1062 (4.837)
40	0.5291 (5.693)	0.3155 (6.372)	0.1065 (5.133)
45	0.5353 (6.932)	0.3212 (8.294)	0.1089 (7.502)

[a] Measured by photographic method

[b] Numbers in parentheses represent % strain value.

In addition to tensile coupons, specimens in the form of filaments have been prepared. These specimens are Dacron fibers of the type used in knitted prosthetic fabrics and will be used to determine whether any changes in tensile properties occur as a result of carbon coating. We also have coated sutures in inventory for similar experiments.

1.8. Galvanic Properties of Composites

Carbon coating may prevent ionic dissolution which occurs with some materials in vivo. The use of carbon composites may also, however, result in the formation of an undesirable electrolytic couple. A recent study has shown that graphite/epoxy composites act as an extremely noble metal when coupled with alloys in neutral 3.5% aqueous NaCl at room temperature. Titanium alloys, including Ti-6Al-4V, and nickel alloys were found to be most compatible with the graphite composite material. We are in the process of assembling a cell to determine the electrical properties of carbon-coated composites in normal saline and simulated physiological fluids. In the meantime, we have supplied carbon/stainless steel, carbon/titanium, carbon/chrome/cobalt alloy, and pure carbon specimens for electrochemical

testing at the University of Alabama. Initial results show that carbon and stainless steel can form a potential couple resulting in corrosion of the stainless steel. Titanium alloys and carbon do not form a couple.

For the past 2 yr, we have been aging partially carbon-coated stainless steel, partially coated titanium, and partially coated chrome/cobalt alloys in normal saline at 80°C. The saline solution is periodically analyzed via atomic absorption for the presence of metallic impurities, i.e., corrosion products. After a period of about 6 months, the saline containing the stainless steel sample was noticeably discolored and the test terminated. The titanium and chrome/cobalt alloy tests are continuing. While this type of test is difficult to quantify in terms of corrosion rate, it does confirm qualitatively the results from the electrochemical tests at the University of Alabama. Carbon/stainless steel composites are no longer being supplied for biological testing, although such specimens had been supplied prior to obtaining these results.

TASK II. PROVIDE CHARACTERIZED SPECIMENS IN VARIOUS FORMS AND ON VARIOUS SUBSTRATES FOR BIOLOGICAL TESTING BY OTHER NHLBI CONTRACTORS

2.1. Summary of Activities

Carbon-coated composites of various forms and other carbon specimens were characterized using optical and scanning electron microscopy, electron microprobe spectroscopy, and Auger electron spectroscopy. These specimens were sent to collaborating contractors of the Biomaterials Program for basic scientific studies and for biological testing. The configuration and geometry of these specimens were dictated in general by specific in-vitro, in-vivo, and ex-vivo testing protocols. In particular, coated polymeric and control specimens were sent to Research Triangle Institute; carbon flow tubes and plates were prepared for use by Calspan Corporation; unalloyed LTI carbon (containing no substrates) was prepared for Avco Everett Research Laboratory; carbon-coated quartz disks and rectangular specimens as well as uncoated controls were sent to the University of Washington; and microfiber scaffolds were coated with carbon and sent to the University of Michigan. Specific details on the test specimens are given in the following paragraphs. Results from testing these specimens and those specimens sent in prior years are presented under Task III.

2.2. Research Triangle Institute

Six-in. square sheets of Kapton (a polyimide) were coated and sent to Dr. H. Yasuda for carbon film permeability measurements. GA previously measured the CO_2 permeability of carbon-coated composites. Dr. Yasuda is extending these initial permeability measurements and is investigating the transport of oxygen, nitrogen, and water vapor through coated composites. In addition to the Kapton specimens we supplied, Dr. Yasuda sent 4-1/4-in. square sheets of polysulfone, polypropylene, mylar, and acrylonitrile-butadiene-styrene (ABS) for coating with varying thicknesses of carbon. The polysulfone, polypropylene, and mylar sheets were coated with nominally 500-Å, 1000-Å, 2000-Å, and 4000-Å-thick carbon films. By using transmitted

light, the coated composites were examined for defects. The defect density followed a consistent pattern. The thinnest coatings exhibited the fewest pinholes. The 1000-Å-thick coatings generally contained the greatest number of defects. The defect density then decreased with increasing film thickness. Polysulfone composites exhibited the fewest defects, from none to on the order of $1/cm^2$. Polypropylene and mylar followed in that order. The ABS polymer was unsuitable for permeability studies. This polymer/carbon composite exhibited the same type of surface cracks characteristic of acrylics and some polyurethanes.

2.3. University of Washington

At Dr. B. Ratner's request, rectangular and circular cover slips were coated, inspected, and sent to the University of Washington for study. Ten coated quartz rectangles (35 mm x 60 mm) along with 10 uncoated control specimens were shipped to Dr. Ratner in October 1977. The 10 coated disks (16 mm in diameter) and their uncoated controls were shipped in November 1977.

2.4. Avco Everett Research Laboratory

Samples of unalloyed LTI carbon and silicon-alloyed LTI carbon were sent to Dr. E. Nyilas earlier. These disk specimens were fabricated by applying a thick coating (∿2 mm) of pure or silicon-alloyed LTI carbon on a 0.1-mm-thick graphite substrate. The resultant coated disks were nominally 97% LTI carbon and 3% graphite. These disks were subsequently ground by Avco to obtain carbon particles suitable for determining the thermochemical parameters describing the adsorption of native proteins on LTI carbon. It was felt, at the time, that the 3% non-LTI-carbon content of the particles would not compromise these experiments. In order to verify this conjecture, pure LTI carbon specimens containing no substrate were fabricated at the request of the Biomaterials Program Manager. These specimens were fabricated in two steps. Graphite disks were first coated with LTI carbon. These coated disks were polished and recoated. By grinding the edges of the twice-coated disks, the interface between the first and second coatings was exposed. The second coating was separated from the first coating, resulting

in thin disk-shaped specimens of pure LTI carbon containing no substrates (i.e., the second coating was free-standing). This was a rather lengthy process, but approximately 10 g of material was prepared and shipped to Dr. Nyilas.

2.5. University of Michigan

Dr. R. Kahn recently reported on pseudointimas produced by seeding various fabrics with WI-38 cells. He found that carbon-coated nylon consistently was the best pseudointimal substrate among the materials tested. However, using transmission electron microscopy, he found the carbon coating to be brittle and subject to phagocytosis. The particular carbon-coated specimens Dr. Kahn used were fabricated several years ago. The carbon coating was anisotropic and consequently expected to be brittle. Carbon coatings currently being produced are isotropic and expected to be less brittle. We have received new disk samples of polyester (polytetramethylene terephthalate) with an impermeable estane backing from Dr. Kahn for coating. Ten disks have been coated and are ready for shipment to Dr. Kahn. Examination of one of the coated disks shows the carbon coating to be uniform and crack-free. Typical SEM photomicrographs are shown in Fig. 2-1.

2.6. Calspan Corporation

At the request of Dr. V. A. DePalma, several types of carbon specimens were fabricated, inspected, and shipped. For testing in Calspan's flow cell, LTI carbon plates having dimensions of 1.005 in. x 0.785 in. were fabricated. These plates were polished, but some of them will be intentionally roughened by Calspan. Fourteen plates were shipped. For comparison with the behavior of LTI carbon plates in Calspan's flow cell, quartz rectangles having identical dimensions were obtained and coated with $\sim$3000 Å of vapor-deposited carbon. These coated specimens are currently being inspected. In an attempt to eliminate any adverse prior blood-surface interactions which may compromise the flow cell results, Calspan requested flared inlet tubes fabricated from LTI carbon. We have fabricated and shipped 10 of these tubes to replace the previously used glass tubes. An additional 10 flared

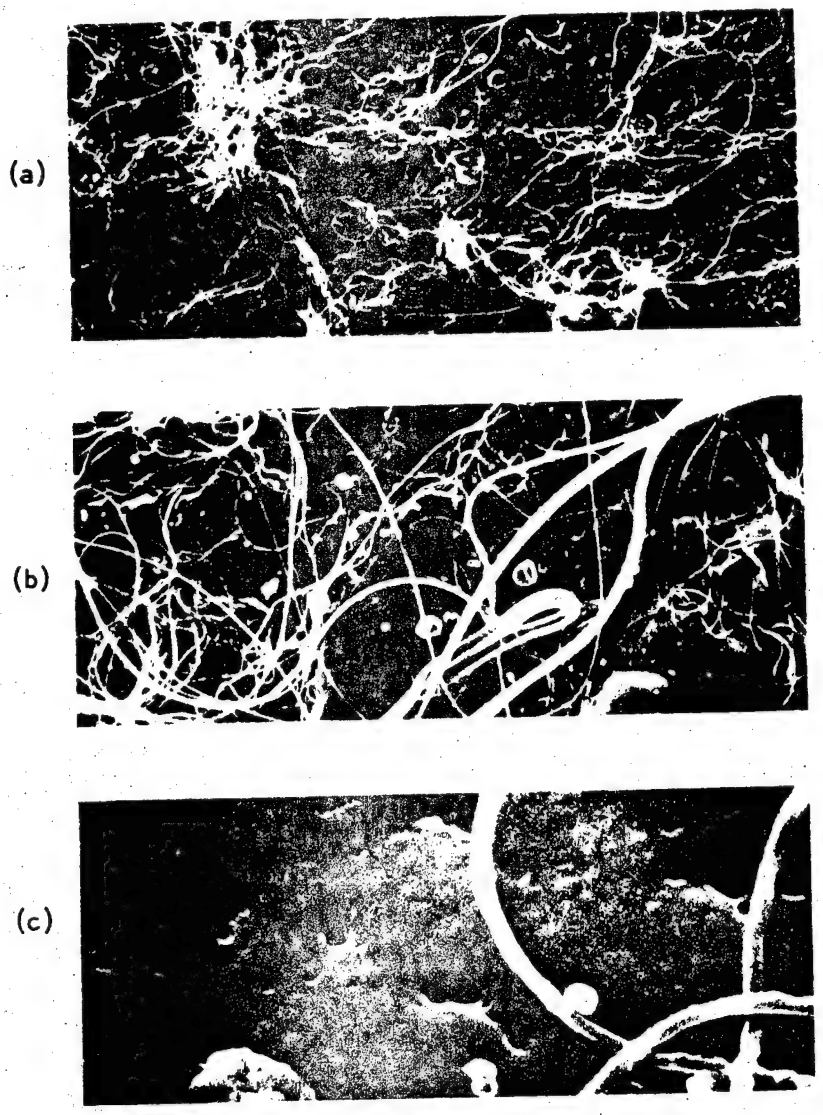


Fig. 2-1. Carbon-coated microfiber scaffolding: (a) 35X; (b) 200X; (c) 5000X

tubes are being fabricated. For another part of their study, Calspan requested and received 12 polished LTI carbon Gott rings. Recently, an additional nine Gott rings were requested. These rings are to have the outside as well as the inlet and outlet flares polished, but the inside of the ring is not to be polished. These nine rings have been completed and are ready for shipment. A graphite sheet (10 cm x 15 cm x 0.05 cm) was also sent during the present reporting period.

2.7. Other Activities

Well-characterized carbon-coated materials have also been sent to other institutions. Carbon-coated membranes and nickel microchannels were sent to the University of Pittsburgh for blood-contacting applications. Extensive surface analyses are being conducted both prior to and after blood contact. Coated electrodes have been sent to the University of Alabama for galvanic potential measurements. Dacron/polyurethane/carbon composites are being evaluated, in dogs, for use in trachea reconstruction. Partially coated cover slips (1/2 coated and 1/2 uncoated) have been sent to the University of Utah for cell adhesion studies. These initial samples were coated with nominally 200 Å and 2000 Å of carbon to determine whether gross differences in cell adhesion are found as a result of the different coating thicknesses.

TASK III. COLLABORATE WITH OTHER CONTRACTORS

3.1. Summary of Activities

Under this task and at the direction of the Biomaterials Program Manager, contact was made with other contractors to coordinate activities, to set guidelines for collaborative efforts, to facilitate biomaterials information exchange, and to learn the results of their tests on GA's samples. During the present reporting period, test results were received from the University of Vermont, Columbia University, UC Berkeley, Research Triangle Institute, Utah Biomedical Test Laboratory, University of Michigan, Calspan Corporation, and Avco Everett Research Laboratory. In addition, biological test data were received from the University of Pittsburgh. Some samples were returned to GA after testing. These specimens are being examined in an effort to analyze the biological test results and to correlate them with the chemical and physical properties of the carbon samples. Specific details are given in the following paragraphs. In many cases, the work outlined is by no means complete and is continuing. The data obtained during the present reporting period continue to show that vapor-deposited carbon composites perform well in the biological environment.

3.2. University of Vermont

Renal embolus test results on five coated stainless steel rings were received from the University of Vermont in July 1977. Their communication of test results to GA can be found in Appendix B. To date, 17 rings have been tested. A summary of all of the results is given in Table 3-1. Individual data on the 17 rings can also be found in Appendix B.

From Table 3-1 it can be seen that thrombotic deposits within the ring lumen were generally quite modest. There were no thickened deposits within any of the rings which markedly reduced the size of the lumen, nor were any of the rings occluded (i.e., none of the 17 rings were judged to be in category 3 or 4). The aorta below the ring was clean in most cases.

TABLE 3-1
SUMMARY OF THROMBOEMBOLIC PATTERNS IN RENAL EMBOLUS TEST SYSTEM[a]

Ring Thrombus[b]	Aorta below Ring	Kidney Infarcts
2 - 0s 8 - 1s 7 - 2s 0 - 3s 0 - 4s	14 - Clean 3 - 3 to 7 mm of thrombotic material adherent to aorta below ring	Variable, from substantial to very modest. Little correlation between extent of renal damage and amount or nature of residual luminal thrombotic material. Carbon surface ranks relatively high in both apparent thromboresistance and embolic propensity.

[a] University of Vermont

[b] Ring thrombus code:
0 = None
1 = Thin coating on ring lumen and/or skimpy deposit in rim/aorta groove
2 = Thin coating on ring lumen which projects from ring in the form of a tube or flag
3 = Thickened deposit on all or part of the ring lumen which markedly reduces size of the lumen and may extend from ring to block or partially block a renal artery
4 = Any thrombus which completely occludes ring lumen

In only three of the 17 rings tested was there any thrombotic material adherent to the aorta, and, in at least one of those cases, the thrombus in the aorta was felt to result from minor damage to the aortic wall sustained during surgery and not from the ring itself. The accompanying infarct damage to the kidneys, according to the University of Vermont findings, was variable, from substantial to very modest. Little correlation was found between the extent of renal damage and the amount of residual thrombotic material in the ring. According to Mr. R. W. Larrow's letter, this observation has been made with many of the other better-performing surfaces which have been encountered at the University of Vermont. The latest series of five rings has been returned to GA for post-implantation study. These rings have been fixed and extracted but have not yet been evaluated.

3.3. Columbia University

In the previous annual report (Ref. 1), the results of experiments at Columbia University on the adhesion of platelets to vacuum-deposited carbon-coated glass cover slips were reported. It was found that the number of platelets adhering to these carbon surfaces was smaller by about a factor of 2 than the number adhering to the standard Stanford Research Institute (SRI) polyether urethane (PEU). Additional experiments to characterize the uptake of human fibrinogen, gamma globulin, and albumin were planned, but these results are not available to date. Columbia University, however, has measured the uptake of platelets on companion LTI carbon disks and has reported (Ref. 5) the results of measurements on 11 disks. None of these samples showed any platelet adhesion.

3.4. UC Berkeley

Hemolysis testing was discussed with Dr. M. C. Williams at the Devices and Technology Branch Contractor's Conference in December 1977. The results from the standard tests were reported earlier (Ref. 1). Dr. Williams' results indicated that shear-induced hemolysis for both LTI

carbons and vacuum-deposited carbons is comparable to that of polyethylene (a low hemolyzer) or even lower when tested to 12,000 sec. At longer times, according to Dr. Williams, the difference between the carbon surfaces and polyethylene became greater. The incremental plasma hemoglobin concentration with the polyethylene continues to increase with time, while with the carbon surfaces the incremental concentration levels off to a steady-state value.

3.5. Research Triangle Institute

Dr. Yasuda has measured the oxygen, nitrogen, and water vapor permeability of a carbon-coated Kapton composite specimen and has reported his results to GA. The composite permeability to oxygen and nitrogen is very low and confirms our earlier experience with oxygen. The water vapor permeability of the composite is measurable. The calculated permeability constant is comparable to that determined in our own laboratory using CO_2. Dr. Yasuda is planning to extend these measurements using the membranes coated with varying thicknesses of carbon described under Task II.

3.6. Utah Biomedical Test Laboratory

Vena cava test results were received in August 1977 on seven vacuum-deposited carbon-coated Ti-6Al-4V titanium alloy rings. Of these specimens, one was not implanted, one was TNV (test not valid), two occluded in 2 hr, one occluded at 2 weeks, and one each was of categories I and O. Unfortunately, none of the tested rings were returned for post-implantation study at GA.

To date, including the above, 19 rings have been implanted. Of these, three were TNVs, five occluded in 2 hr, three occluded during the 2-week test period, and eight were open after 2 weeks (i.e., two of category I and six of category O). This is a consistent pattern irrespective of the substrate employed and shows that the initial implantation period is critical. Rings tested according to this protocol that remain patent for

2 hr generally remain patent for 2 weeks. According to Dr. A. U. Daniels' August 1977 letter, these results indicate that the surface is relatively thromboresistant in the manner of other extremely smooth surfaces; i.e., the specimens either clot rapidly or stay relatively clot-free for the 2-week test period, with little tendency toward intermediate results.

3.7. University of Michigan

Testing of carbon-coated stainless steel shafts according to the University of Michigan's ex-vivo protocol continued during the present reporting period. In their most recent annual report, normalized data on the performance of this composite material and that of uncoated shafts were tabulated. The carbon coating resulted in a dramatic decrease in clot formation and clot composition when compared with the uncoated shafts. However, because of test variability and the number of samples tested (12 shafts), the statistics comparing the performance of carbon-coated shafts and that of the standard silastic shafts are not very definitive. Dr. J. S. Schultz recommended that additional tests be performed. Since the finding was made that carbon-coated stainless steel may be unsatisfactory in the biological environment, arrangements will be made with Union Carbide to obtain some of their molded polypropylene shafts for coating and subsequent testing at the University of Michigan.

3.8. Union Carbide Corporation

From discussions with Mr. D. Stewart, it was learned that Union Carbide has developed a mold and is producing polypropylene shafts of the type used in the University of Michigan's ex-vivo blood compatibility experiments. Mr. Stewart offered to make these shafts available to GA. A formal request for 30 shafts will be issued shortly.

3.9. Calspan Corporation

Dr. DePalma informed GA in November 1977 (see Appendix C) of potential difficulties with the glass entry and exit portions of Calspan's flow

cells and inquired whether tubes of a more thromboresistant material (e.g., LTI carbon) could be fabricated. Ten tubes were shipped in January 1978. Implantation of Calspan's flow cells for material characterization, including the smooth and roughened LTI carbon surfaces and the vapor-deposited carbon/quartz surfaces described under Task II, has been halted until receipt of the carbon tubes because of concern about the effect of adverse blood-surface interactions prior to entry into the flow cell on the results in the flow cell. With inlet and outlet tubes now in Calspan's possession, these experiments should begin again shortly. Dr. DePalma also informed GA of the performance of two LTI carbon rings implanted by Dr. V. L. Gott in the inferior vena cava. Both rings were open after two weeks. One had a very small thrombus in the dependent portion, and the other a moderate thrombus according to Dr. Gott's evaluation.

3.10. Avco Everett Research Laboratory

Considerable data have been generated by Avco on the behavior of varous carbon samples tested according to the SPFE protocol, in their microcalorimeter, and from electrophoretic mobility measurements. Some of the results have been published (Refs. 6-9). A request for a summary of the results has been sent to Dr. Nyilas.

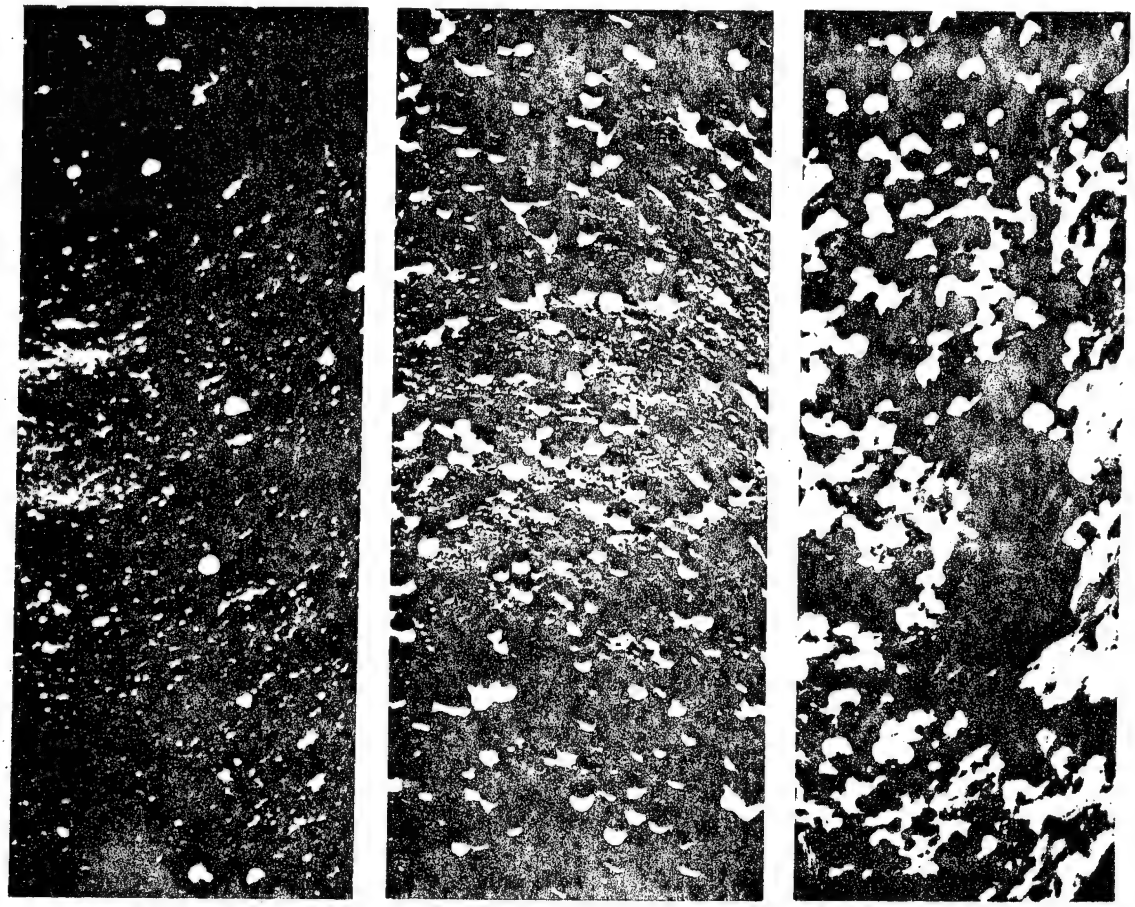
3.11. University of Washington

Dr. Ratner has performed some preliminary experiments with the carbon-coated quartz specimens described under Task II. He informed GA of some difficulty in observing cells on the black opaque surface similar to difficulties encountered by others when evaluating opaque specimens. He is modifying his experimental protocol to overcome the problems associated with specimen opacity.

3.12. University of Pittsburgh

In collaboration with a group at the University of Pittsburgh, data have been obtained comparing the deposition of cellular blood elements on several metal surfaces including nickel surfaces coated with vacuum-deposited carbon. The test surfaces form part of a microchannel extracorporeal perfusion system. In recent comparative experiments, the cellular deposition on bare nickel, TDMAC-heparin-coated nickel, and carbon-coated nickel microchannels were evaluated and reported (Ref. 10). Shown in Fig. 3-1 are photomicrographs (500X) of these three test surfaces after 4 hr of perfusion. It should be noted that the cracks in the TDMAC-heparin surface are thought to be an artifact of specimen preparation.

There are striking differences in the number of platelets adhering to the test surfaces. The bare nickel and the TDMAC-heparin-coated nickel surfaces show a uniform distribution of adherent platelets. Platelet adhesion to the carbon-coated surface is minimal. This finding is consistent with other studies performed over a much shorter blood-contacting period. It is also interesting to note that platelet adhesion to the carbon-coated surface in this experiment was minimal, in spite of the fact that the test surface was relatively rough.



(a) (b) (c)

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Fig. 3-1. Deposition of cellular blood elements following 4 hr of blood perfusion (500X): (a) carbon-coated nickel; (b) bare nickel; (c) TDMAC-heparin-coated nickel. (Courtesy University of Pittsburgh.)

TASK IV. PRODUCTION OF "STANDARD" VENA CAVA AND RENAL EMBOLUS IMPLANT RINGS FOR USE BY CONTRACTORS OF THE BIOMATERIALS PROGRAM

4.1. Summary of Activities

At the direction of the Biomaterials Program Manager, GA has prepared, inspected, and shipped vena cava and renal embolus implant rings for use by collaborating contractors. During the present reporting period, we have supplied approximately 950 test rings for use by others. The injection mold was completed and accepted. Rings were molded from Pellethane-D, polypropylene, ethylene/vinyl acetate copolymer, polycarbonate, and polysulfone. The molded rings have a much smoother surface topography than the earlier machined rings, as evidenced by inspection at GA and at collaborating institutions. The smooth topography should be an advantage to most contractors. Some contractors, however, require a rough topography to promote adhesion of their test materials to the rings. In those cases, the ring surface is rendered matt through light grit blasting with sodium bicarbonate. Several hundred of each type of molded ring are currently in inventory.

4.2. Injection Molding of Rings

In an effort to provide standard test rings for use by NHLBI contractors of the Biomaterials Program, GA in the past has machined Delrin, polypropylene, polystyrene, and polycarbonate vena cava and renal embolus implant rings using our standard shop procedures. At the direction of the Biomaterials Program Manager, GA machined, inspected, and distributed the rings to other contractors, along with the relevant quality control records. For cases in which the rings were used as substrates for SRI's PEU, the rings were first sent to SRI for coating and then returned to GA for inspection and distribution to those NHLBI contractors who required the PEU surface for grafting of their test materials.

Because of the cost and lead time required for machining substrates and coating with PEU, injection molding of implant rings was pursued as

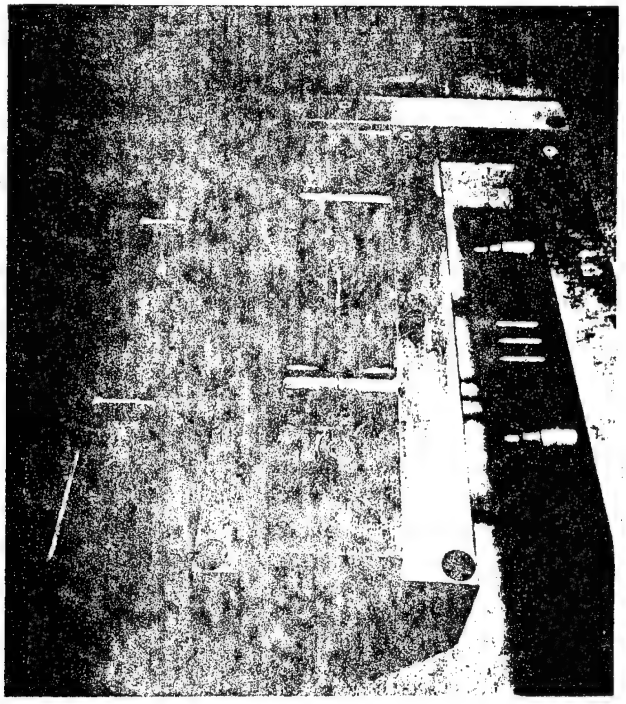
an alternative to the machining/coating process. After a formal review, an injection molding vendor was chosen and a mold was constructed (see Fig. 4-1). The mold has two cavities so that a vena cava ring and a renal embolus ring are produced in a single cycle. The initial samples produced in the mold showed areas that needed rework. This work has been completed. The mold has been accepted. Approximately 500 vena cava and renal embolus rings were molded from five different polymers: namely, polypropylene, polycarbonate, Pellethane-D, polysulfone, and ethylene/vinyl acetate copolymer. Representative samples of these rings have been inspected for surface finish. The rings have been inventoried. Individual rings are inspected prior to shipment.

4.3. Ring Characterization

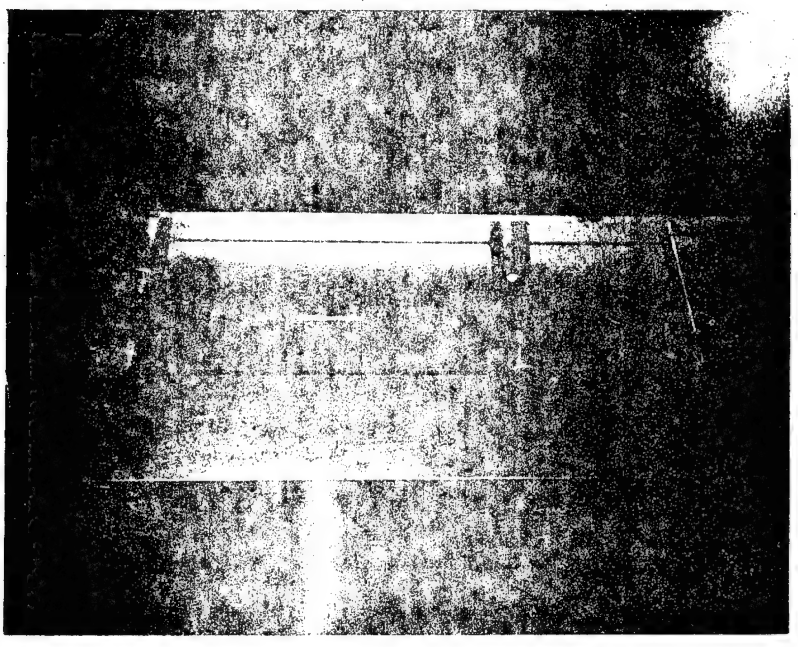
Representative samples of both types of rings from each of the above-mentioned polymers were examined at GA using optical and scanning electron microscopy. In addition, we have received the results of inspection by other contractors, notably Dr. G. Kwiatkowski at Union Carbide and Dr. Yasuda at Research Triangle Institute.

As can be seen in Fig. 4-1, the mold is a two-part mold. The major imperfections in the molded rings resulted from difficulties in accurately mating the two halves. By lapping the two halves in a single unit, these imperfections were minimized. The general surface topography of the molded rings is far smoother than the typical as-machined surface. SEM photomicrographs obtained from Union Carbide and representative of these two types of surfaces are shown in Fig. 4-2. The machined surface in the past was considerably smoothed by thick test material coatings applied by the colloborating contractors. Some contractors, however, requested rings intentionally roughened through microsandblasting to enhance coating adhesion, so the smoother topography of the molded rings may be an advantage for some contractors but a disadvantage for other contractors.

Surface textural irregularities have been shown to have a pronounced effect on blood tolerability of artificial surfaces. Recent vena cava

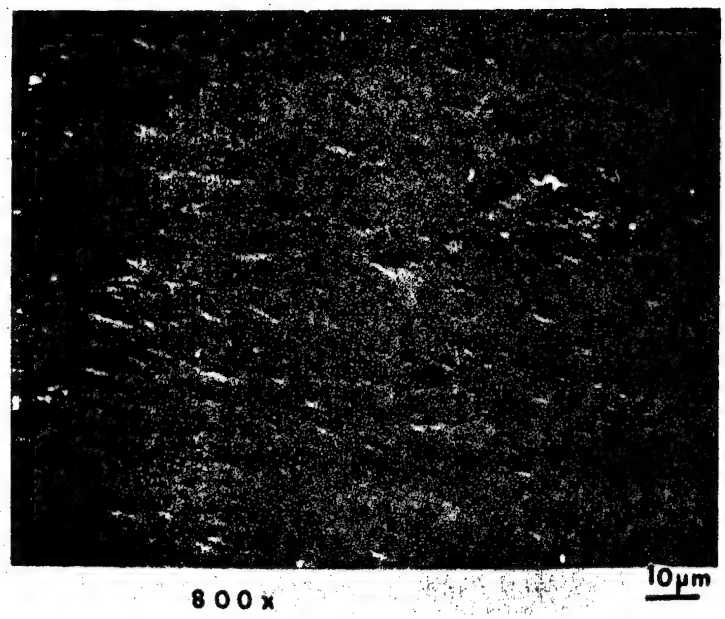


781327 (a)



781326 (b) EL-2962

Fig. 4-1. Injection mold for fabrication of implant rings: (a) mold disassembled; (b) partially assembled. Top cover removed to show mold cavities.



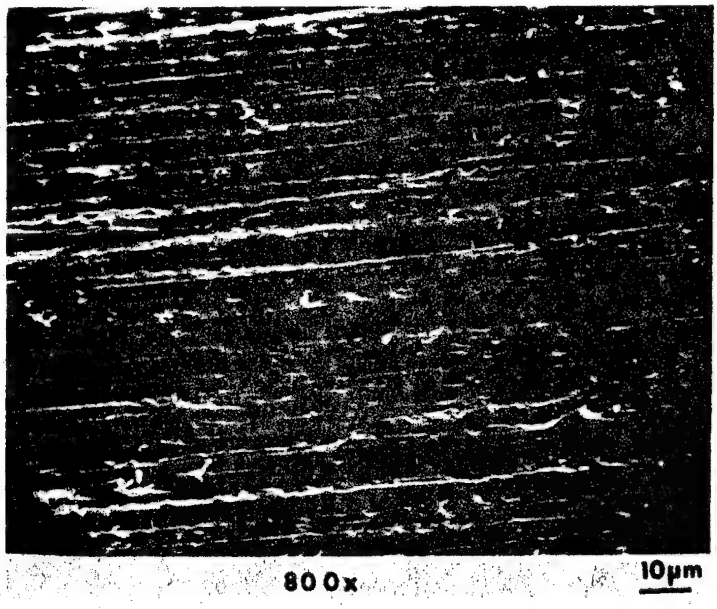


Fig. 4-2. SEM photomicrographs of interior of standard implant rings: (a) new molded rings; (b) old machined rings. (Courtesy Union Carbide Corporation.)

tests at the Utah Biomedical Test Laboratory have shown a striking difference between the performance of uncoated machined polypropylene rings and that of uncoated molded polypropylene rings. Test results from a series of 10 machined rings yielded two TNVs, seven X-2H, X-ED, or X-2W, and only one Category I, while a similar series with molded rings yielded only two X-2H or X-2W and seven category I or 0. These rings were steam-autoclaved. Similar results were obtained with an EtO sterilized series.

Toxicity testing was carried out at the University of Tennessee on 200 molded Pellethane-D rings. Dr. J. Autian indicated that some leachable constituents were present in the rings, in particular when nonaqueous extracts were used. Dr. Autian's results can be found in Appendix D. In general, the material was found to be noncytotoxic and nonhemolytic, was tolerated systemically, and did not inhibit cell growth. Only the intradermal test in rabbits of PEG 400 and the cottonseed oil extracts produced a low order of irritancy. The saline extract did not show a response. The overall cummulative toxicity index was calculated to be 180, which is higher than the generally assumed value of 100 or less characterizing materials deemed acceptable for biomedical applications in regard to acute toxicity.

Because of the indication that leachable constituents are present, in particular when nonaqueous extracts are used, 40 molded Pellethane-D rings were shipped to Polysciences for leachable extraction experiments. We are conducting parallel experiments and will submit extracted rings to Dr. Autian for additional toxicity testing.

4.4. Ring Disbursement

Vena cava and renal embolus rings of Delrin, Pellethane-D, polypropylene, polycarbonate, and ethylene/vinyl acetate copolymer were prepared and shipped to collaborating contractors of the Biomaterials Program at the direction of the Biomaterials Program Manager. Table 4-1 lists the recipients of the more than 950 rings processed by GA during the present reporting period.

TABLE 4-1
VENA CAVA (VC) AND RENAL EMBOLUS (RE) RINGS
SUPPLIED TO NHLBI CONTRACTORS

Contractor	Number and Ring Type	Material
Gulf + Western	40 VC	Polypropylene
	40 RE	Polypropylene
Utah Biomedical Test Laboratory	20 VC	Polypropylene
	140 VC	Polycarbonate
Calspan Corporation	12 VC	LTI carbon
Stanford Research Institute	60 VC	Delrin
	48 RE	Delrin
North Star	20 VC	Delrin
	20 RE	Polypropylene
Polysciences	20 VC	Pellethane-D
	20 RE	Pellethane-D
Franklin Institute	20 VC	Polypropylene
	20 RE	Polypropylene
University of Tennessee	100 VC	Pellethane-D
	100 RE	Pellethane-D
Research Triangle Institute	110 VC	Polypropylene
	50 RE	Polypropylene
Union Carbide Corporation	20 VC	Polypropylene
	40 RE	Polypropylene
	20 VC	Ethylene/vinyl acetate
	20 RE	Ethylene/vinyl acetate
University of Washington	17 VC	PEU-coated Delrin
	16 RE	PEU-coated Delrin

ACKNOWLEDGMENTS

The authors gratefully acknowledge the review and comments of J. C. Bokros and the assistance of J. B. Horsley and P. A. Salvatierra. D. R. Wall is thanked for the electron microscopy, and D. P. Snowden and R. Densen are thanked for the Auger spectroscopy.

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2. Shim, H. S., and A. D. Haubold, "The Fatigue Behavior of Vapor-Deposited Carbon Films," General Atomic Report GA-A14515, December 1977 (submitted to J. Bioeng.).
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9. Nyilas, E., and T. H. Chiu, "Adsorption Properties of Human γ-Globulin on Pure and Silicon-Alloyed LTI Carbons," in Extended Abstracts, 13th Biennial Conference on Carbon, Irvine, California, July 1977, p. 85.

10. Borovetz, H. S., et al., "A Scanning Electron Microscopic Study of Blood-Material Interfaces in Extracorporeal Capillary Flow" (to be published in Transactions of International Conference on X-Ray Optics and Microanalysis).

APPENDIX A

PUBLICATIONS DURING PRESENT REPORTING PERIOD BASED IN PART ON WORK SPONSORED BY THIS CONTRACT

Haubold, A. D., "Carbon in Prosthetics," Ann. N. Y. Acad. Sci. 283, 383 (1977).

Shim, H. S., N. K. Agarwal, and A. D. Haubold, "Fatigue Behavior of Thin Carbon Films," in Extended Abstracts, 13th Biennial Conference on Carbon, Irvine, California, July 1977, p. 140.

Agarwal, N. K., H. S. Shim, and A. D. Haubold, "The Adhesion of Thin Vacuum-Deposited Carbon Films," in Extended Abstracts, 13th Biennial Conference on Carbon, Irvine, California, July 1977, p. 338.

Shim, H. S., N. K. Agarwal, and A. D. Haubold, "The Microstructure of Vapor-Deposited Carbon Films," in Extended Abstracts, 13th Biennial Conference on Carbon, Irvine, California, July 1977, p. 428.

Shim, H. S., and C. H. Meyer, Jr., "The Microstructure of Isotropic Vapor-Deposited Carbon Films," J. Bioeng. 1, 99 (1977).

Shim, H. S., and A. D. Haubold, "The Wear Behavior of Vacuum-Vapor-Deposited Carbon Films," General Atomic Report GA-A14740, November 1977 (submitted to J. Bioeng.).

Borovetz, H. S., et al., "SEM and Surface Analytic Study of an Isotropic Vapor-Deposited Carbon Film on Microporous Membranes," presented at American Scanning Electron Microscopy Symposium, April 1978 (to be published in the proceedings).

Shim, H. S., and A. D. Haubold, "The Fatigue Behavior of Vapor-Deposited Carbon Films," General Atomic Report GA-A14515, December 1977 (submitted to J. Bioeng.).

Shim, H. S., and A. D. Haubold, "The Adhesion of Thin Carbon Films to Various Substrates," presented at 4th Annual International Biomaterials Symposium, April 1978.

Shim, H. S., C. H. Meyer, Jr., and A. D. Haubold, "Gaseous Flow through Thin Carbon Films," General Atomic Report GA-A14833, February 1978 (submitted to J. Bioeng.).

APPENDIX B

RENAL EMBOLUS TEST RESULTS FROM UNIVERSITY OF VERMONT

The University of Vermont
DEPARTMENT OF PATHOLOGY
MEDICAL ALUMNI BUILDING, BURLINGTON, VERMONT 05401

July 14, 1977

Dr. A. Haubold
General Atomic Company
P. O. Box 81608
San Diego, CA 92138

Dear Dr. Haubold:

Enclosed are data and comments pertaining to a series of vacuum-deposited carbon coated stainless steel rings received for evaluation. Also included are diagrams depicting the distribution of thrombotic material observed on the ring surface and a photograph of a representative postmortem specimen. Five of the rings were appropriately rinsed and gluteraldehyde fixed and returned to you today for further examination. They were refrigerated until the time of shipment to delay mold or bacterial growth.

After two to four days of implantation, the thrombotic deposits within the ring lumen were observed to be generally quite modest, oriented toward one or both of the rims, and loosely adherent to the surface. The color was noted to be light tan or pink on the thinner deposits and darker on the thicker accumulations.

The accompanying infarct damage to the kidneys was variable, from substantial to very modest. There appears to be little correlation between the extent of renal damage and the amount or nature of the residual luminal thrombotic material. This observation has been made with many of the other better-performing surfaces which we have encountered.

Sincerely,

Rodney W. Larrow

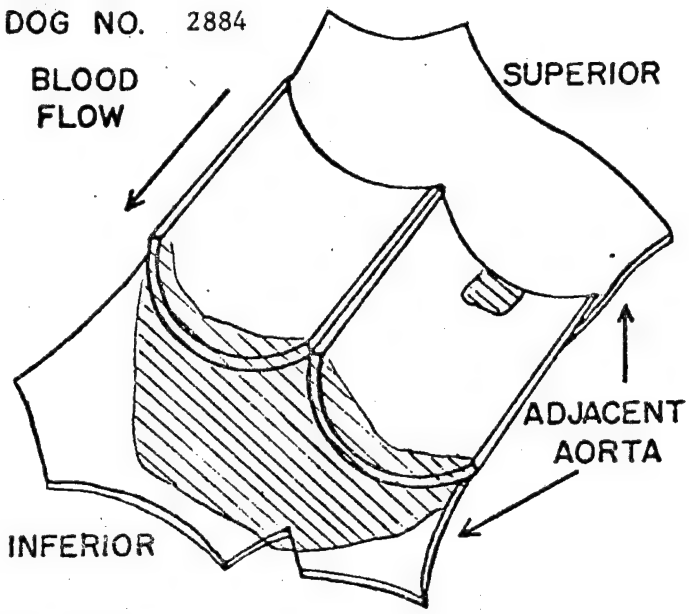
Rodney W. Larrow

RWL/mcw

DISTRIBUTION OF RING IMPLANT THROMBI

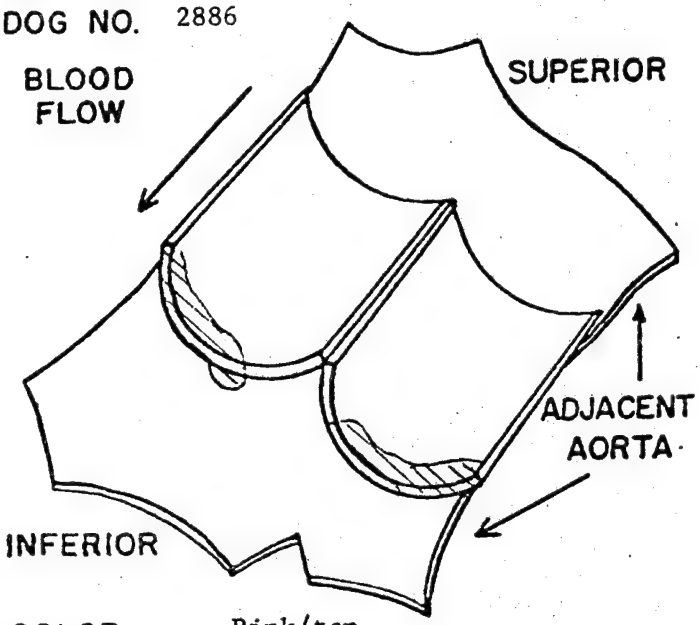
General Atomic Company

RING NO. 3
DOG NO. 2884



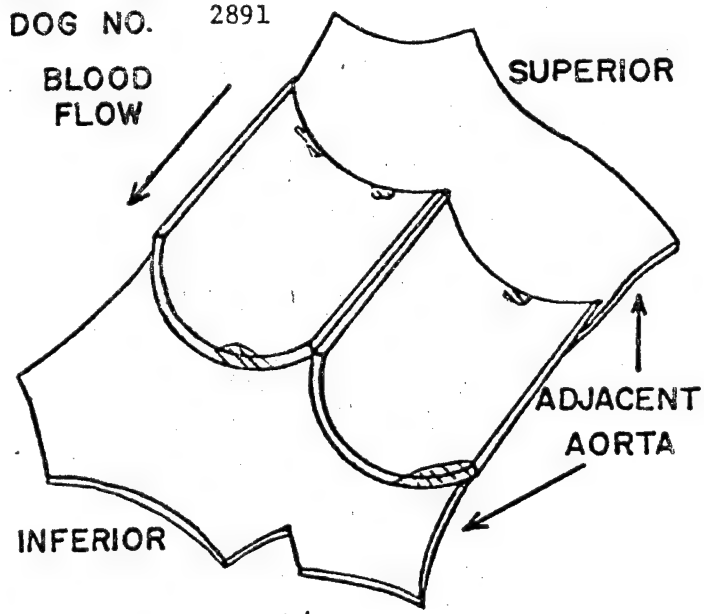
COLOR Tan/red
TEXTURE Uneven
THICKNESS To 2 mm.
DEGREE OF ADHERENCE TO RING SURFACE Very loose
RING THROMBUS CODE 2

RING NO. 6
DOG NO. 2886



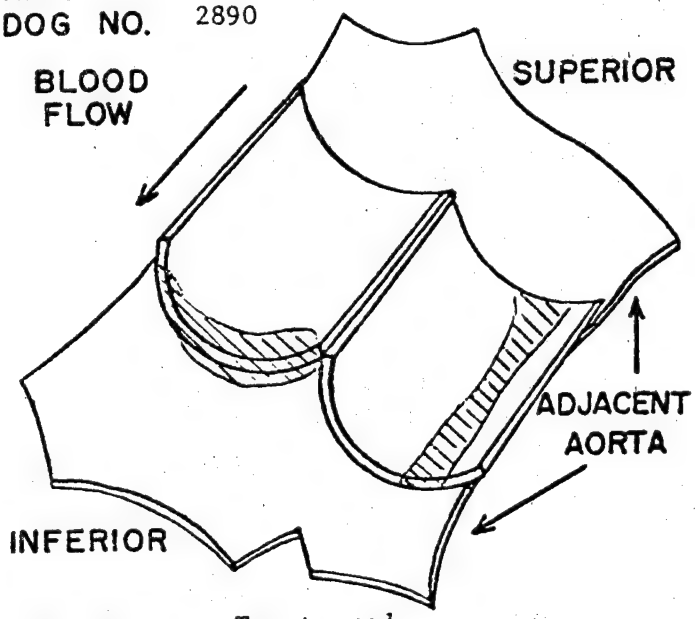
COLOR Pink/tan
TEXTURE Uneven
THICKNESS <1 mm.
DEGREE OF ADHERENCE TO RING SURFACE Loosely
RING THROMBUS CODE 1-

RING NO. 1
DOG NO. 2891



COLOR Pink/tan
TEXTURE Uneven
THICKNESS <1 mm.
DEGREE OF ADHERENCE TO RING SURFACE Loosely
RING THROMBUS CODE 1-

RING NO. 2
DOG NO. 2890

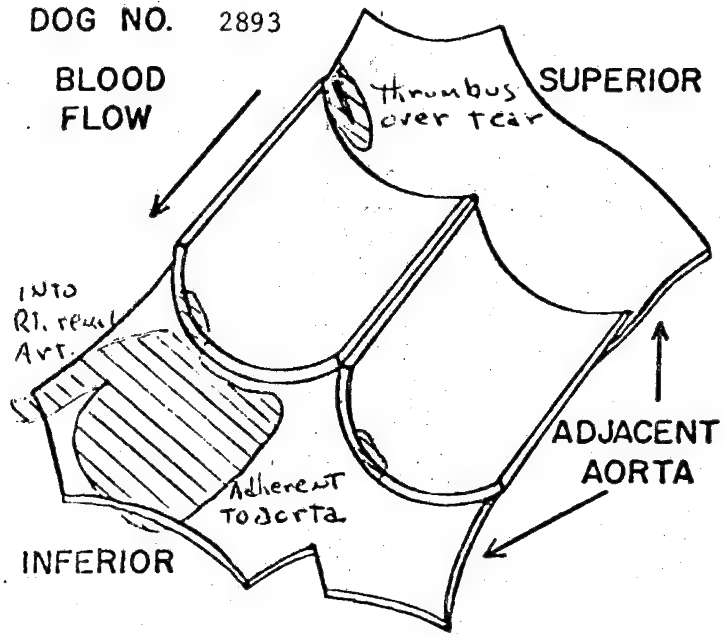


COLOR Tan to red
TEXTURE Uneven
THICKNESS To 1 mm.
DEGREE OF ADHERENCE TO RING SURFACE Loosely
RING THROMBUS CODE 2-

DISTRIBUTION OF RING IMPLANT THROMBI

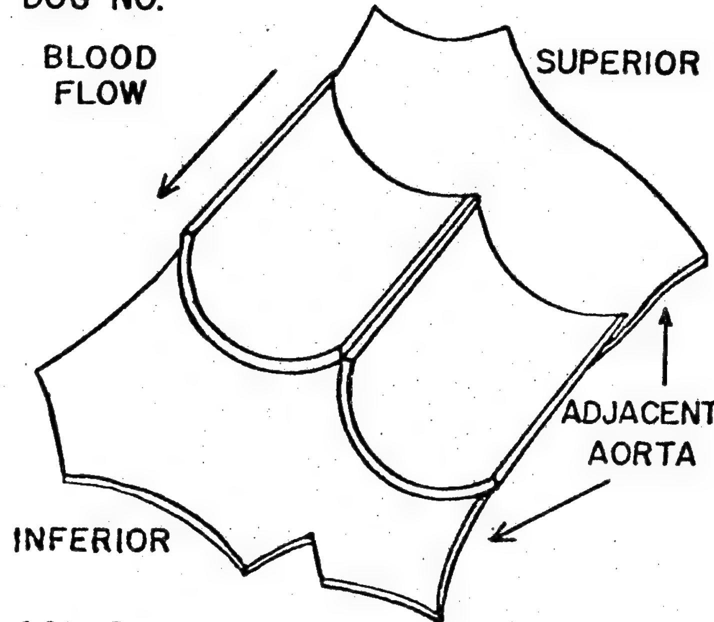
General Atomic Company

RING NO. 4
DOG NO. 2893



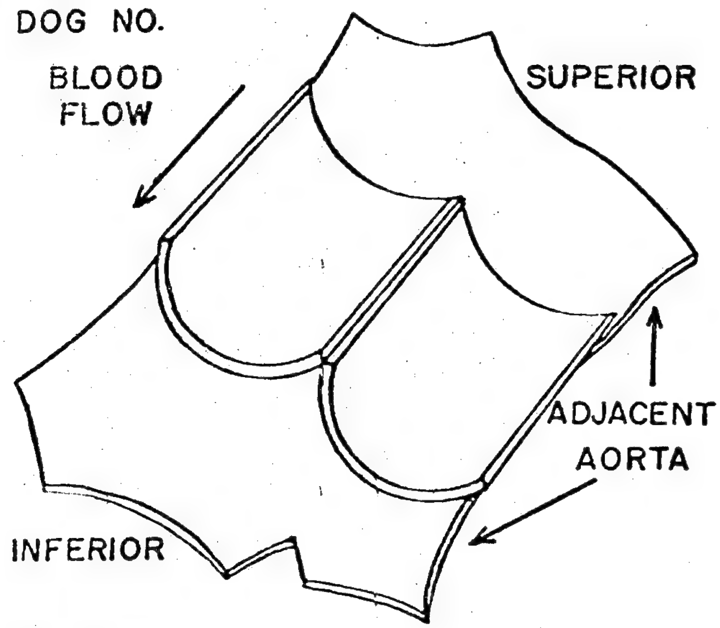
COLOR Red/tan
TEXTURE Smooth granular
THICKNESS <1 mm.
DEGREE OF ADHERENCE
TO RING SURFACE Loosely
RING THROMBUS CODE 1-

RING NO.
DOG NO.



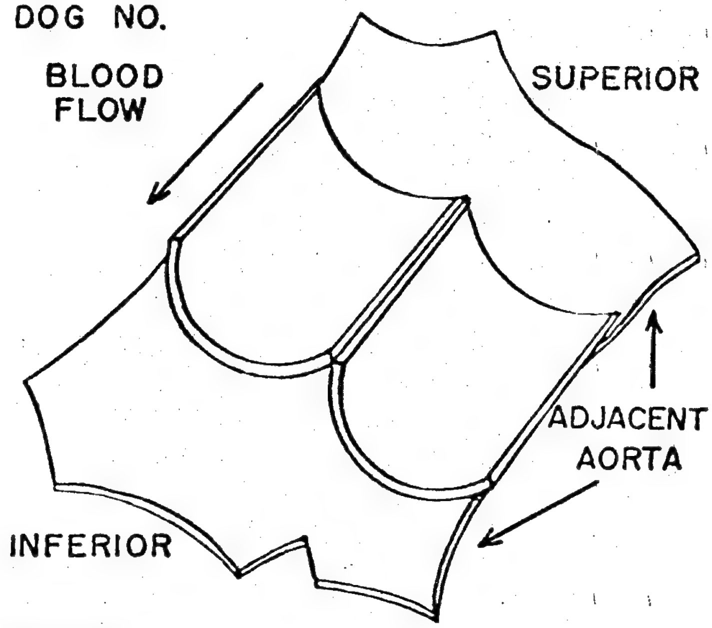
COLOR
TEXTURE
THICKNESS
DEGREE OF ADHERENCE
TO RING SURFACE
RING THROMBUS CODE

RING NO.
DOG NO.

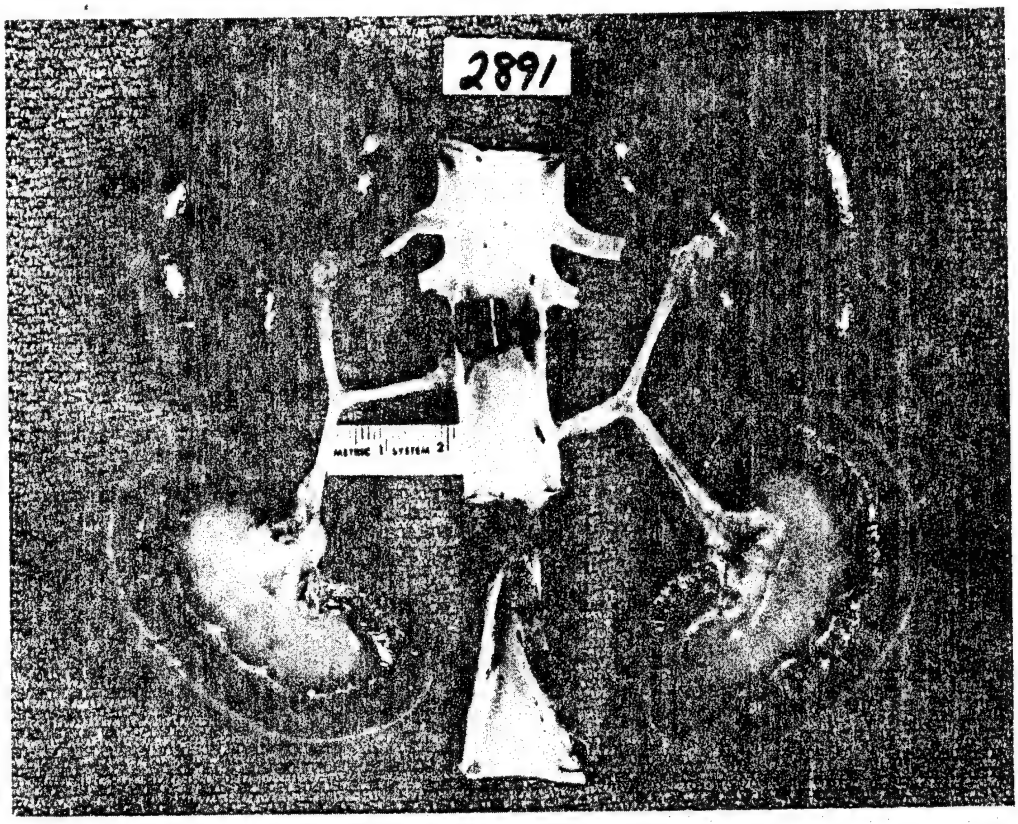


COLOR
TEXTURE
THICKNESS
DEGREE OF ADHERENCE
TO RING SURFACE
RING THROMBUS CODE

RING NO.
DOG NO.



COLOR
TEXTURE
THICKNESS
DEGREE OF ADHERENCE
TO RING SURFACE
RING THROMBUS CODE



781233 EL-2964

Fig. B-1. Dog No. 2891: dissected renal embolus test system. (Courtesy University of Vermont.)

Ring material:	Stainless-steel-coated with vacuum-deposited carbon, steam autoclave sterilized
Implant duration:	3 days
Ring thrombus code:	1-
Right kidney:	Three infarcts, the largest being 6 mm
Left kidney:	None grossly visible

TABLE B-1
THROMBOEMBOLIC PATTERNS OBSERVED WITH
CANDIDATE MATERIALS FROM GENERAL ATOMIC COMPANY

Dog No.	Date	Materials Code[a]	Duration	Ring Thrombus Code[b]	Aorta below Ring	Kidney Infarcts
2884	6-28-77	1	3 days	2	Clean	Right: Substantial infarct damage Left: Substantial infarct damage
2886	6-29-77	1	2 days	1-	Clean	Right: One 2-mm infarct Left: Three infarcts, <1 mm
2891[c]	7-5-77	1	3 days	1-	Clean	Right: Three infarcts, the largest being 6 mm Left: None grossly visible
2890	7-6-77	1	2 days	2-	Clean	Right: One 6-mm infarct Left: None grossly visible
2893[d]	7-11-77	1	4 days	1-	7 mm x 5 mm clot from rim to right renal artery	Right: Five infarcts, 3 to 15 mm Left: Two infarcts, 2 and 4 mm

[a] Materials code:
1 = Stainless-steel-coated with vacuum-deposited carbon, steam autoclave sterilized

[b] Ring thrombus code:
0 = None
1 = Thin coating on ring lumen and/or skimpy deposit in rim/aorta groove
2 = Thin coating on ring lumen which projects from ring in the form of a tube or flag
3 = Thickened deposit on all or part of the ring lumen which markedly reduces size of the lumen and may extend from ring to block or partially block a renal artery
4 = Any thrombus which completely occludes ring lumen

[c] See Fig. B-1.

[d] In this case, most of the thrombus in the aorta above and below the ring arose from minor damage to the aortic wall sustained during surgery and not from the ring itself.

TABLE B-2
SUMMARY OF THROMBOEMBOLIC PATTERNS OBSERVED[(a)]
WITH CANDIDATE MATERIALS FROM GENERAL ATOMIC COMPANY

Duration	Ring Thrombus Code	Aorta below Ring	Kidney Infarcts
3 days	1	Clean	Right: Two infarcts, 8 mm or smaller Left: Same
4 days	1-	Clean	Right: One 2-cm infarct, suspicious areas Left: Several small suspicious areas
3 days	0	Clean	Both kidneys 50% damaged by infarcts
3 days	1-	Clean	Two to four very small suspicious areas in both
5 days	2-	Clean	Right: Numerous infarcts, substantial damage Left: One 4-mm infarct, many suspicious areas
3 days	1-	Clean	Right: Numerous infarcts up to 1 cm Left: Five to six infarcts up to 8 mm, other suspicious areas
4 days	1-	Clean	Right: Four to six infarcts up to 5 mm Left: One 2-mm infarct Many suspicious areas in both
3 days	2+	Thrombotic material adherent to aorta 3 to 4 mm below ring	Right: Numerous large and small infarcts Left: Many infarcts
5 days	2+	Clean	Right: Many infarcts, near total damage Left: Numerous large and small infarcts
5 days	0	Clot-covered circumferential laceration 5 mm below left renal artery	Right: Numerous infarcts up to 2 cm Left: Eight to ten infarcts up to 4 mm
3 days	2	Clean	Right: 80% infarcted Left: Ten to twelve infarcts up to 6 mm

(a) University of Vermont

TABLE B-2 (continued)

Duration	Ring Thrombus Code	Aorta below Ring	Kidney Infarcts
3 days	2	Clean	Right: Many infarcts Left: Twelve or more infarcts up to 8 mm
3 days	2	Clean	Right: Substantial infarct damage Left: Substantial infarct damage
2 days	1-	Clean	Right: One 2-mm infarct Left: Three infarcts, <1 mm
3 days	1-	Clean	Right: Three infarcts, the largest being 6 mm Left: None grossly visible
2 days	2-	Clean	Right: One 6-mm infarct Left: None grossly visible
4 days	1-	7 mm x 5 mm clot from rim to right renal artery	Right: Five infarcts, 3 to 15 mm Left: Two infarcts, 2 and 4 mm

APPENDIX C

COMMUNICATION OF TEST RESULTS AND REQUEST FOR FLARED INLET TUBES FROM CALSPAN CORPORATION

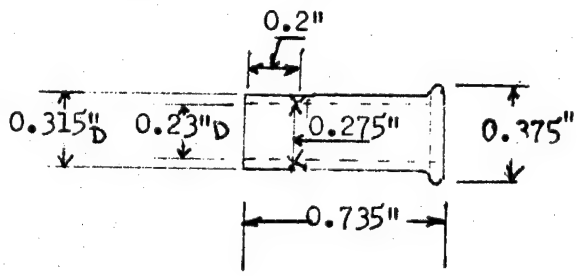
Calspan

November 2, 1977
VAD:bjs

Dr. Axelrod Haubold
Gulf Atomic Company
Gulf Energy & Environmental Systems
P. O. Box 81608
San Diego, California

Dear Dr. Haubold:

As you know we have been working with Dr. Gott, who is implanting our flow cells containing the pyrolytic carbon plates which you prepared for us under our collaborative N.I.H. contracts. These flow cells are molded of a silicone compound which I believe is fairly thromboresistant. The amount of blood contact with the silicone material is severely limited by the design of the cell. On the other hand, this is not true for the inlet tubes used to connect the flow cell to the animal's circulation. The dimensions of these tubes are given in the figure below.



Recently, Dr. Gott raised a very serious consideration concerning the blood interaction of smooth and roughened pyrolytic carbon plates in these flow cells in view of the possible interaction of the blood with the inlet tubes which are currently constructed from glass. The nature of his comment is noted in the last paragraph of a letter recently forwarded to us, a copy of which is included for your review. As a result of Dr. Gott's comment, Bob Baier and I have been considering modifications to the flow cell which might be made to ensure that the actual materials under study were the pyrolytic carbon plates of various surface roughness. It is our opinion that inlet and outlet tubes made of smooth pyrolytic carbon would most likely reduce, if not eliminate, any adverse prior blood-surface interactions. In addition, if this approach could be implemented, it would permit the construction of the cell from only two materials, carbon and silicone rubber.

Would you let me know if you can fabricate pyrolytic carbon tubes having the dimensions indicated in the above figure. If you can, I would like 20 of them. I have enclosed a sample of a glass tube which works well in the flow cells under discussion. The tolerance of the tubes can be taken as ± .005". Your efforts in helping us with this aspect of our work will be greatly appreciated.

Sincerely,

Vito DePalma

Vito A. DePalma, Ph.D.
Principal Physicist
Environmental & Energy Systems Department

enc

cc: Dr. V. Gott
Dr. S. Bruck
Dr. R. Baier

THE JOHNS HOPKINS UNIVERSITY
SCHOOL OF MEDICINE

DEPARTMENT OF SURGERY
Cardiovascular Surgery Service

Please address reply care of:
THE JOHNS HOPKINS HOSPITAL
BALTIMORE, MARYLAND 21205

Vincent L. Gott, M.D.
Robert K. Brawley, M.D.
James S. Donahoo, M.D.
Timothy J. Gardner, M.D.
J. Alex Haller, Jr., M.D.

October 26, 1977

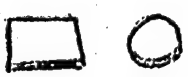
Vito A. DePalma, Ph.D.
Principal Physicist
Calspan Corporation
Post Office Box 235
Buffalo, New York 14221

Dear Vito:

I wanted to summarize the results of some of our recent implants of Calspan devices that were carried out here in our laboratory.

We have recently returned to you two pyrolytic carbon rings implanted in the inferior vena cava for a two-week period. Ring #1 was implanted on September 14, 1977, and the animal was sacrificed on September 28, 1977. That animal weighed 27 lbs. and the ring had a very small thrombus in the dependent portion. A diagram of the thrombus is depicted below. Ring #2 was implanted on September 16, 1977, and the animal was sacrificed on September 30, 1977. The animal weighed 28 lbs., and the ring had a medium sized thrombus on the dependent inflow end of the ring. The degree of thrombus is depicted in the diagram below.

I was a little surprised that there was a moderate thrombus in Ring #2, although the fact that the ring was patent indicates that it has good thromboresistance. In the past, the majority of our pyrolytic carbon rings implanted for two weeks have been free of thrombus at the end of this period. As you know, only materials with very excellent thromboresistant properties remain free of thrombus for a two-week period when placed as a ring in the inferior cava.



On September 22, 1977, you sent us three flow cells for implantation in the inferior renal vena cava. These implantations were carried out on October 4, 1977. Implantation was performed by our research associate in charge of the laboratory, Dr. Patrick Magee, under my supervision. First of all, we found the coils are still somewhat bulky and difficult to implant. In fact, with the implantation of Cel #3 (roughened pyrolytic carbo.: plates), we had to leave the inferior vena cava clamped for a few minutes while we dissected the cava above and below the cell to allow room for insertion of the entry and exit tubes into the vein. When we took the clamp off, there was some clot in the cava below the cell and this then flowed into the device. As you know, Dr. Magee called you at the time this occurred, and you felt that it was still reasonable to have this coil returned to you as a control coil with early thrombus. Again, though, the thrombus originated from the inflowing cava and it was a fa or in the thrombus that was observed within the cell.

Cells #1 and #2 were also implanted on October 4, 1977. Implantation of these two cells went much more smoothly. They were filled with saline prior to implantation to eliminate any air-blood interface. It was hard, of course, to determine exactly when thrombus occurred in the cells because of the nature of their design, but it appeared that thrombus occurred in Cell #1 between the third and fourth hours and in Cell #2 between the second and fourth hours. The cells were actually implanted for a total of four hours, and then when removed were rinsed with physiologic saline and then flushed with the 3% buffered glutaraldehyde solution. The cells were then wrapped in sterile gauze, placed in the plastic bottle, and shipped back to your lab on the morning of October 5, 1977.

As we discussed on the phone, I think that there could well be a problem in the design of these cells, in that the entry and exit channels are constructed of a material that is not particularly thromboresistant. Certainly, thrombus could be initiated at these sites. I think that you could have the world's best thromboresistant material located in the center of a blood streaming cell and we could not appreciate the degree of thromboresistance of that material if the blood sees a thrombogenetic material as it enters the cell. Obviously, it is ideal that the blood see only the test material and not flow over other materials, particularly on the entry side of such a device. Hopefully, your next cells can be modified so that these factors can be taken into consideration.

Sincerely yours,

Vincent Gott

Vincent L. Gott, M.D.

VLG:bls
CC: Dr. Patrick Magee

APPENDIX D

TOXICITY TEST RESULTS RECEIVED FROM UNIVERSITY OF TENNESSEE ON RINGS MOLDED FROM PELLETHANE-D

Dr. Axel Harbold, Manager
Research & Development
Medical Products Division
General Atomic
11388 Sorrento Valley Road
San Diego, California 92121

August 26, 1977

Project Number: PT 0.1513 NHLBI-FDA (Letter of July 11, 1977)

NOTE: Details of testing procedures for all of the tests described in this report are attached.

A. Sample Tested

Y-5619 Pellethane (2363-55D)

B. Tests Directly on Material

1. Tissue Culture-Agar Overlay Test
   Y-5619 ..... Noncytotoxic (0/0)
   Values of (0/0) and/or (1/0) are recorded as noncytotoxic. Values above these are recorded as cytotoxic.

2. Rabbit Muscle Implant (One Week)
   Y-5619 ..... Gross: 0 (nontoxic, equivalent to negative control)
   Histopathology: 1 (very slight toxic reaction)

3. Hemolysis Test (Rabbit Blood)
   Y-5619 ..... 0% Hemolysis

C. Tests on Extracts

Note: The test sample was extracted with saline, polyethylene glycol 400 and cottonseed oil at 121° C for one hour. Each of the extracts was then tested as indicated below.

1. Tissue Culture-Agar Overlay Test
   Results are summarized in Table I. None of the extracts were recorded as producing a cytotoxic response.

2. Intradermal Test in Rabbits
   Results are summarized in Table I. Both the PEG 400 and the cottonseed oil produced a low order of irritancy. The saline extract did not shown a response.

3. Systemic Toxicity in Mice

Results are summarized in Table I. None of the extracts produced an adverse effect or deaths when injected into mice.

D. Inhibition of Cell Growth Test on Aqueous Extracts

1. Procedure. Various weights of sample per 20 ml. of distilled water were extracted in an autoclave at 121° C for one hour, and then the extracts were included in the cell growth inhibition test.

2. Results. These are shown in Figure 1. As may be noted, none of the extracts with the different sample weights exceeded ± 10% inhibition. Values less than 29% inhibition are considered as not being significant.

E. Cummulative Toxicity Index

The Cummulative Toxicity Index was calculated to be 180. It is generally assumed that values of 100 or less would indicate the material is acceptable for biomedical applications in regard to acute toxicity. It should be pointed out that the concept of the Cummulative Toxicity Index will be re-evaluated as more biomaterials are tested.

F. Remarks

In previous tests Pellethane was found to be a nontoxic material. In the case of Pellethane tested and reported here, there was some indication that leachable constituents were present, in particular, when nonaqueous extracts were used. It would seem prudent for a new sample of this material to be re-tested to confirm the responses noted in this report.

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TABLE I

SUMMARY OF TEST RESULTS ON EXTRACTS
SAMPLE Y-5619

Extract	Tissue Culture	Intradermal Test (Rabbits)	Systemic Toxicity (Mice)
Saline	NC (1/0)*	0**	0/5***
PEG 400	NC (1/0)	2	0/5
Cottonseed Oil	NC (1/0)	1	0/5

* Indicates Noncytotoxic

** Response recorded from 0 (nonirritating) to 3 (equivalent to positive control response)

*** Indicates that no adverse effects or deaths were caused in five injected mice.

INHIBITION OF CELL GROWTH ASSAY (ICG)

FIGURE: 1 : **Y-5619 Pelethane Sample 2363-55D**

The x-axis indicated the quantity of material extracted at 121°C, 1 hour, in distilled water. The assay is based on relative growth at 72 hours in the presence and absence of the extract, distilled water control.